Neurocognition of Developmental Dyslexia:
The Role of Multisensory Processing During Reading and Spelling

Thesis

presented to the Faculty of Arts

the University of Zurich

for the Degree of Doctor of Philosophy

by

Monika Kast

Citizen of Rehetobel AR

Accepted in the fall semester 2010
on the recommendation of

Prof. Dr. rer. nat. Lutz Jäncke
PD Dr. rer. nat. Martin Meyer

Zurich 2011

Acknowledgment

There are many people I would like to thank for supporting me in the various phases of my PhD. Only a few of them will be named here. I am painfully aware that there are so many more very important people for whom these words cannot express the gratitude and respect I feel.

First of all, I thank my supervisors Prof. Lutz Jäncke and Dr. Martin Meyer for giving me the opportunity to carry out this dissertation on a topic of my choice. I am so very grateful for their scientific guidance and mentoring. I would like to convey my appreciation for their competent advisory, their professional support, and their fruitful scientific stimulation. I have truly enjoyed working in the Department of Psychology at the University of Zurich.

Further, I like to express great thanks to my coworkers at the Institute of Neuropsychology, for their encouragement as well as for creating a friendly and cheerful atmosphere. Special thanks go to the auditory group, and especially to my office colleague, Dr. des. Stefan Elmer. Their collective helpful comments on my work contributed greatly, and the overall interesting and stimulating atmosphere made the time spent a pleasure. Additionally, a warm thank goes to Ladina Bezzola for her patience and helpfulness, and for providing me with knowledge of fMRI data acquisition and analysis.

I would like to convey my gratitude for the collaborative efforts of the Zurich-based ETH Institute for Computational Science. An especially great thank-you goes to Prof. Markus Gross, for providing me the initial project and encouraging me to begin a PhD. Moreover, I would like to thank the ETH PhD student Gian-Marco Baschera for the inspiring, productive and fruitful team work. I greatly enjoyed his friendly, comradery and essential help.

I offer my gratitude to the people working at Dybuster AG and especially to Christian Vögeli and Mirjam Flühler, whom accompanied me professionally and offered personal friendship.

Last but not least, a warm thank-you goes to my family and my relatives who have supported me in so many ways. I am particularly indebted to my friends for sharing so many nice and inspiring times as well as enriching and cheerful moments. Special thanks go to James Perry for supporting and encouraging me with his love as well as for providing English language proof reading and critical comments.

Table of Contents

List of Abbreviations

A	Auditory
ANOVA	Analysis of variance
AG	Angular gyrus
AV	Audiovisual
AVc	Audiovisual congruent
AVi	Audiovisual incongruent
BOLD	Blood oxygen level dependent
EEG	Electroencephalography / electroenephalogram
ERP	Event related potential
DD	Developmental dyslexia
DTI	Difussion tensor imaging
FA	Fractional anisotrophy
fMRI	Functional magnetic resonance imaging
GFP	Global field power
GM	Grey matter
IPS	Intraparietal sulcus
ISI	Inter stimulus interval
MEG	Magnet encephalogrphy
PET	Positron emission tomography
PT	Planum temporale
RAN	Rapid automatized naming
SMG	Supramarginal gyrus
STS	Superior temporal sulcus
V	Visual
VBM	Voxel-based morphometry
WM	White matter

Summary

Reading and spelling skills are essential in modern societies, where information is commonly provided by written media. In the case of developmental dyslexia (DD) the acquisition of these essential techniques is reduced. Individuals affected by DD are characterized by low spelling and writing skills in spite of having an average IQ, good educational support and a solid social background (World Health Organization, 1993). Although contemporary researchers benefit from several decades of research in the field of DD, the causes of spelling and reading failure are still debated. Various theories exist, which focus on the general auditory (Baldeweg, Richardson, Watkins, Foale, & Gruzelier, 1999; Reed, 1989; Tallal, 1980), visual (Livingstone & Hubel, 1988; Lovegrove, Bowling, Badcock, & Blackwood, 1980; Stein & Walsh, 1997), combined auditory and visual (Farmer & Klein, 1995), or motor impairments (Nicolson & Fawcett, 1990; Rudel, 1985; Wolff, Michel, & Ovrut, 1990) dyslexic individuals often suffer from. The most accepted theory is the phonological processing deficit hypothesis (Bradley & Bryant, 1983; Ramus et al., 2003b). This theory suggests a specific impairment in the representation, storage and/or retrieval of speech sounds (Bradley et al., 1983; Ramus et al., 2003b) as well as a reduced phoneme to grapheme mapping skills, which are essential for reading and spelling (Frith, 1985).
The purpose of the present work was to investigate the phonological processing and especially the phoneme to grapheme conversion in dyslexic and non-dyslexic children and adults. Consequently, the four experiments reported in this thesis were designed by using functional techniques such as electroencephalography (EEG) and functional magnet resonance imaging (fMRI). Additionally, we analyzed behavioral data of children working for three months with a computer-based spelling learn program.

The aim of **experiment I**, entitled ‘ERP Differences of Pre-Lexical Processing between Dyslexic and Non-Dyslexic Children’ was to examine the ‘pre-lexical component’. The ‘pre-lexical component’ or N170 occurs approximately 170 ms after visually presented words, pseudowords, strings of consonants and strings of alphanumeric symbols as a sharp negative going wave-form (Bentin, Mouchetant-Rostaing, Giard, Echallier, & Pernier, 1999; Rossion, Joyce, Cottrell, & Tarr, 2003). This component reflects the conjunction of the grapheme with the corresponding phoneme (Maurer, Brem, Bucher, & Brandeis, 2005) and also the experience-dependent neural changes of visual expertise (Nobre, Allison, & McCarthy, 1994). Our data yielded that children with DD exhibit reduced neuronal responses over occiptiotemporal electrodes on the left hemisphere for both words and pseudowords, and on the right hemis-

phere for pseudowords. These reduced responses reflect the reading difficulties of dyslexic children and the specific component sensitive and essential for the processing of print, which also is dependent on accumulated experience. It can be concluded that dyslexic children are characterized by slower plastic reorganization over the occipitotemporal brain area that is important for acquiring fluent reading skills. Additionally, our data revealed bilateral processing of words and pseudowords irrespective of groups. This finding supports the assumption that neuronal reorganization is necessary and that reading experience drives progressive specialization of a pre-existing leftward inferior temporal pathway dedicated to visual object recognition (Brem et al., 2006; McCandliss & Noble, 2003b; Polk et al., 2002).

Reading can be considered as an audiovisual task whereas the visually presented grapheme has to be transformed into the corresponding sound representation. **Experiment II,** an EEG-study, entitled 'Impaired Audiovisual Integration of Linguistic Contents in Dyslexic Adults' and **experiment III,** a fMRI-study, entitled 'Multi- and unisensory decoding of words and nonwords result in differential brain responses in dyslexic and non-dyslexic adults' were designed to investigate audiovisual processing of phonological information in dyslexic and non-dyslexic adults. The data of the EEG-study revealed in dyslexic adults enhanced mean amplitudes of the global field power (GFP) for both the audiovisual congruent and audiovisual incongruent condition in a time range at about 400 to 600 ms. This result indicates in dyslexics impaired audiovisual integration of phonological information in a time window sensitive for processing semantic information. The enhanced neuronal responses were associated with different topographic maps between dyslexics and non-dyslexics individuals. This result might reflect that in non-dyslexic adults words are better represented in the orthographical lexicon and therefore more sensitive to process semantic information. This reasoning is in line with the phonological deficit theory (Bradley et al., 1983; Ramus et al., 2003b). Additionally, in the time window overlapping with the N170 component during processing visually presented nouns, the dyslexic adults showed stronger GFP magnitudes, when compaired to non-dyslexic individuals. We suggest that this finding reflects reduced proficiency in mastering the phoneme to grapheme mapping. We assume that we did not find different neuronal responses between groups in the time window of the N170 in the audiovisual conditions due to the fact that the visual impairment was compensated by the auditory information.

The behavioral data collected during the fMRI experiment demonstrated no group differences, either for accuracy or for reaction time. Contrarily, non-dyslexics compared to dyslexic adults, elicited stronger hemodynamic responses in the leftward supramarginal gyrus (SMG) as well as in the right hemispheric superior temporal sulcus (STS). The involvement of a dor-

sal and ventral pathway during reading and processing speech is in line with several previous findings (Hickok & Poeppel, 2007). Additionally, our data yielded a significant group by condition interaction in the rightward anterior insula, which indicates that dyslexics have difficulties in processing auditory information.

Our EEG and fMRI-studies evidenced that dyslexic compared to non-dyslexic adults recruit bimodal neuronal circuits specialized for processing phonological information differently. To date the underlying mechanism is not fully understood. It is possible that impairments in one modality influencee the other modality. The interaction of the neurons from one or several impared unisensory areas may cause abrrerant responses in the multisensory area. Also, there may be poorly modulated interaction and processing of those multimodal components. Thus the poor phoneme to grapheme mapping and, in turn, word decoding, might be caused by these aberrant responses in multimodal areas.

Alternatively, it could be that dyslexic individuals developed per se less neurons in bimodal areas which are sensible for processing phonological information. Therefore, less efficient bimodal circuits might have cause impaired phoneme to grapheme conversion and therefore reading problems.

The results of experiments I-III indicate the association of DD with a phonological impairment. In accordance with the phonological deficit theory, makers of a spelling-focused learning program designed specifically for dyslexic children expanded the framework of the learning software by including two phoneme-based adjustments. To aid readers in visualizing phonemes, an additional non-verbal code was implemented. Also, the "word selection controller" was adjusted to reflect a phoneme-based student model, which allows adaptation to individual spelling difficulties. **Experiment IV**, entitled 'Computer Based Learning of Spelling Skills in Dyslexic and Non-Dyslexic Children' was designed to investigate the spelling behavior of dyslexic and non-dyslexic children. The results offer evidence that dyslexic children benefit significantly from the additional phonological code and the corresponding phoneme-based student model. Actually, dyslexics improved their spelling skills to the same extent as non-dyslexics and were able to memorize phoneme to grapheme correspondence when given the right support and adequate training. Furthermore, children with low attention functions benefit from the structured learning environment. Generally our data showed that memory sources are supportive cognitive functions for acquiring spelling skills and for using the information cues of a multimodal learning environment.

Zusammenfassung

Das Beherrschen von Lese- und Rechtschreibfähigkeiten ist in unserer modernen Gesellschaft von zentraler Bedeutung, denn Informationen werden vorwiegend in geschriebener Form übermittelt. Der Erwerb von Lese- und Rechtschreibfertigkeiten ist bei Personen, die von der Entwicklungsdyslexie (Lese- und Rechtschreibstörung) betroffenen sind, jedoch reduziert. Das Defizit kann jedoch nicht auf einen verminderten IQ, mangelnde schulische Ausbildung oder ein schwieriges, soziales Umfeld zurückgeführt werden. Obschon seit mehreren Jahrzehnten die Entwicklungsdyslexie intensiv erforscht wird, sind der genaue Pathomechanismus und die Ätiologie unklar. Es liegen mehrere Theorieansätze vor, welche in ihren Modellen die allgemeinen auditorischen, visuellen, sensorischen oder motorischen Beeinträchtigungen, die bei Dylektikern auftreten, versuchen zu erklären. Die phonologische Defizithypothese gilt als die anerkannteste Theorie. Diese besagt, dass die Lese- und Rechtschreibstörung durch spezifische Schwierigkeiten in der Repräsentation, der Encodierung und/ oder im Abruf von phonologischer Information charakterisiert ist. Weiter manifestiert sich das phonologische Defizit in einer reduzierten Phonem-Graphem-Konversion. Das Beherrschen der Phonem-Graphem-Konversion bildet die Grundlage für Lesen und Schreiben.

Die vorliegende Arbeit zielt darauf ab, die phonologische Verarbeitung und insbesondere die Phonem-Graphem-Konversion bei Kindern und Erwachsenen mit einer Lese- und Rechtschreibstörung zu untersuchen. Somit enthält die vorliegende Arbeit vier Experimente, welche mittels Elektroencephalographie (EEG) und funktionelle Magnet Resonanz Tompgraphie (fMRT) Gruppenunterschiede untersuchen. Weiter werden Verhaltensdaten von Kindern, welche während drei Monaten mit einem Rechtschreibprogramm gearbeitet hatten, analysiert.

Experiment I mit dem Titel ‘ERP Differences of Pre-Lexical Processing Between Dyslexic and Non-Dyslexic Children’ untersucht die prälexikalische Komponente zwischen Kindern mit und ohne Lese- und Rechtschreibstörung. Die prälexikalische Komponente, welche auch N170 genannt wird, tritt rund 170 ms nach der visuellen Darbietung von Wörtern, Pseudowörtern, aneinandergereihten Konsonanten und aneinandergereihten alphanumerischen Symbolen als in negativer Richtung ausschlagende Welle auf. Diese Komponente widerspiegelt einerseits Prozesse der Verbindung des Graphems mit dem korrespondierenden Phonem und andererseits die von dem Training abhängigen neuronalen Veränderung visueller Expertise. Unsere Resultate zeigen, dass bei Kindern mit einer Lese- und Rechtschreibstörung die neuronale Antwort über okzipitotemporale Elektroden auf der linken Hemisphäre sowohl für Wörter als auch Pseudowörter und rechts für Pseudowörter reduziert ist. Somit widerspiegelt diese ver-

minderte neuronale Aktivität in einer für die Verarbeitung von geschriebenen Buchstaben- oder Zeichenfolgen sensitiven Komponente, die als Funktion von Expertise moduliert ist, die Lesebeeinträchtigungen von Kindern mit einer Lese- und Rechtschreibstörung. Es kann darauf geschlossen werden, dass bei Dyslektikern die plastische Reorganisation über okzipitotemporalen Regionen langsamer stattfindet. Denn insbesondere linkseitige okzipitotemporale Regionen sind für effizientes Lesen verantwortlich. Weiter zeigen unsere Daten, dass sowohl Kinder mit als auch ohne Lese- und Rechtschreibstörung Wörter und Pseudowörter bilateral verarbeiten. Dieser Befund untermauert die Annahme, dass effizientes Lesen neuronale Reorganisation erfordert. Weiter weist er darauf hin, dass die Leseerfahrung eine progressive Spezialisierung auf bereits vorher vorhandenen linksseitigen inferior temporalen Bahnen hervorruft.

Weil Lesen als eine bimodale Aufgabe betrachtet werden kann, bei dem das visuell präsentierte Graphem in das korrespondierende Phonem überführt werden muss, wurden zwei Experimente zur Untersuchung audiovisueller Verarbeitung von phonologischer Information geplant. Beim **Experiment II** mit dem Titel 'Impaired Audiovisual Integration of Linguistic Contents in Dyslexic Adults' handelt es sich um eine EEG-Studie. **Experiment III** ist eine fMRT-Studie mit dem Titel 'Multi- and unisensory decoding of words and nonwords result in differential brain responses in dyslexic and non-dyslexic adults'. Bei beiden Studien wurden Erwachsene mit und ohne Lese- und Rechtschreibströung untersucht und verglichen. Die Ergebnisse der EEG-Studie wiesen bei den Dyslektikern eine erhöhte mittlere Amplitude der Feldstärke (global field power (GFP)) sowohl für die audiovisuell kongruente als auch audiovisuell inkongruente Bedingung auf. Diese erhöhten Amplituden traten in einem Zeitfenster von rund 400 bis 600 ms nach der Darbietung des Reizes auf, welches semantische Verarbeitung widerspiegelt. Weiter waren die stärkeren Amplituden mit unterschiedlichen Topographien zwischen Erwachsenen mit und ohne Lese- und Rechtschreibströrung assoziiert. Es liegen Hinweise vor, dass bei Erwachsenen ohne Leseschwierigkeiten Wörter besser repräsentiert sind und somit diese in der Verarbeitung von semantischer Information sensitiver sind. Diese Betrachtungsweise geht mit der phonologischen Verarbeitungsdefizithypothese einher. Weiter konnten wir bei Dyslektikern eine erhöhte Amplitude der N170 bei der ausschliesslich visuellen Wortdarbietung feststellen. Wir gehen davon aus, dass dies die reduzierte Fertigkeit im Umgang mit der Graphem-Phonem-Abbildung und daher die Leseschwierigkeiten darstellt. Weil wir bei den audiovisuellen Bedingungen keinen Gruppenunterschied in der N170 beobachten konnten, gehen wir davon aus, dass das visuelle Defizit mittels auditorischer Information kompensiert werden konnte.

Beim fMRT Experiment zeigen die Verhaltensdaten weder in der Genauigkeit noch in der Reaktionszeit einen Gruppenunterschied. Im Gegensatz zu den Verhaltensdaten wiesen die bildgebenen Verfahren Gruppenunterschiede auf. Die Kontrollpersonen zeigten eine stärkere hämodynamische Antwort im linksseitigen Gyrus supramarginalis sowie im superioren temporalen Sulcus auf der rechten Hemisphäre. Bereits frühere Studien konnten belegen, dass sowohl dorsale als auch ventrale Bahnen für die Verarbeitung von Sprache und Lesen miteinbezogen sind. Zudem stellten wir eine signifikante Interaktion in zwischen der Gruppe und Bedingung in der Insula auf der rechten Hemisphäre fest. Dabei wurde deutlich, dass bei Dyslektikern die Verarbeitung von auditorischer Information beeinträchtigt ist.
Unsere EEG und fMRT Studien zeigten, dass Personen mit einer Lese- und Rechtschreibstörung unterschiedliche bimodale neuronale Netzwerke, welche für die Verarbeitung von phonologischer Information verantwortlich sind, einbeziehen. Der dafür verantwortliche Mechanismus ist bis anhin jedoch noch nicht vollständig geklärt. Es ist zu erwägen, dass Defizite in einer Modalität sich auf die andere Modalität auswirken könnten und dass die Interaktion der beiden Modalitäten sich in assoziativen Regionen niederschlägt. Somit hätten unisensorische Defizite abnorme neuronale Aktivitäten in den bimodalen Konvergenzzonen, welche für die Phonem-Graphem-Konversion beim Lesen verantwortlich sind, hervorgerufen. Alternativ könnte argumentiert werden, dass Dyslektiker per se weniger spezialisierte Neurone in assoziativen Regionen, welche effizientes Lesen ermöglichen, entwickelten. Somit hätten ineffiziente bimodale Netzwerke die Schwierigkeiten in der Phonem-Graphem-Konversion und somit im Lesen verursacht.

Die Ergebnisse der Experimente I-III konnten zeigen, dass die Entwicklungsdyslexie mit phonologischen Beeinträchtigungen assoziiert ist. Der phonologischen Defizittheorie entsprechend wurde bei einem Rechtschreiblernprogramm das Theoriekonzept um zwei weitere Anpassungen erweitert. Beide Anpassungen basieren auf phonologischer Information. Einerseits wurde ein phonologischer Code, welcher die Phoneme mit einem non-verbalen Code visualisiert, implementiert. Andererseits wurde die Steuerung der Wortauswahl dahingehend verändert, dass die phonologischen Schwierigkeiten erkannt und dementsprechend Wörter aufgrund der spezifischen Probleme des Benutzers ausgewählt wurden. Somit zielte das **Experiment IV** mit dem Titel ‘Computer Based Learning of Spelling Skills in Dyslexic and Non-Dyslexic Children’ darauf ab, das Rechtschreiblernverhalten von Kindern mit und ohne Lese- und Rechtschreibstörung zu untersuchen. Die Befunde zeigen, dass Dyslektiker bedeutend vom zusätzlichen Phonologischen Code sowie von der Steuerung der Wortauswahl profitieren. Weiter konnte beobachtet werden, dass dyslektische Kinder dieselben Lernfortschritte wie

Kinder ohne Lese- und Rechtschreibstörung machen können. Dies weist darauf hin, dass Dyslektiker genauso fähig sind, die richtige Wortform sowie Rechtschreibregeln zu lernen, wenn ihnen eine adäquate Unterstützung angeboten wird. Weiter stellten wir fest, dass insbesondere Kinder mit Aufmerksamkeitsschwierigkeiten von der Lernsoftware profitieren. Es kann davon ausgegangen werden, dass ihnen die klare Struktur und Führung, welche die Software bereitstellt, geholfen und sie ihm seriellen Verhalten des Schreibens unterstützt haben könnte. Allgemein wiesen unsere Daten darauf hin, dass Gedächtnisfunktionen beim Lernen der Rechtschreibung eine entscheidende Rolle spielen, denn insbesondere Kinder mit guten verbalen Gedächtnisfunktionen profitieren von den Informationen, welche die Lernsoftware anbietet.

1 Introduction

1.1 Definition of Developmental Dyslexia

Developmental Dyslexia (DD) is characterized by an unexpected difficulty in learning to read and spell in spite of a normal or above average intelligence, good educational support and a solid social background (World Health Organization, 1993). DD is a specific learning disability; affected individuals have inconsistent orthography in spelling as well speed and accuracy problems while reading (Goswami, 2003). Children who fail to achieve normal reading performances show low speed and poor accuracy; visual confusion between morphologically similar letters, especially those having a symmetrical counterpart, such as “b” and “d” or “m” and “n”; inversion, omission, substitution and additions of letters and/or syllables; difficulty in generalizing previously learned grapheme to phoneme rules (especially for complex letter clusters) as well as limited reading comprehension. Spelling difficulties are characterized by: defective spatial arrangement of letters, inversions, omissions and substitutions of letters and/or syllables; inconsistent errors (in spite of enormous training in spelling is the child not able to spell correctly); difficulties in copying texts and writing their own texts as well as week grammatical development (Habib, 2000).

DD exhibits a lifelong persistence rather than a transient developmental lag (Shaywitz, Lyon, & Shaywitz, 2006; Svensson & Jacobson, 2006), and treatments are, in the case of DD fundamental in establishing successful skill acquisition. The special treatments are often longstanding and often seek to minimize the degree of impairments, rather than provide a complete solution for attaining normal reading skills. After several years of conventional efforts, not without unavoidable psychological consequences, reading becomes possible, although often in a clumsy and effortful manner characterized by persistent errors, especially with irregular or exceptional words. Also persistent is a reduced performance in the area of comprehension. The common outcome in adolescence and adulthood is a pronounced spelling impairment (Treiman, 1985), which persists as an indicator for retrospective diagnosis of dyslexia in adulthood (Habib, 2000).

DD is widespread and probably the most common neurobehavioral disorder, affecting over 80% of those identified as learning disabled (Lerner, 1989). The prevalence, ranging from 5% to 17.5% (Shaywitz, 1998), is associated with the deepness of the orthography. It is suggested that in the German speaking region about10% of the population is affected with DD (Rüsseler, 2006). DD occurs more frequently in males (from 2:3 to 4:5, depending on the study).

Dyslexic symptoms are often associated with deficits in related domains such as oral language acquisition (dysphasia), writing abilities (dysgraphia and misspelling), mathematical abilities (dyscalculia), motor coordination (dyspraxia), postural stability and dexterity, temporal orientation (dyschronia), visuospatial abilities (developmental right-hemisphere syndrome), and attentional abilities (hyperactivity and attention deficit disorder) (Gross-Tsur, Manor, & Shalev, 1996; Gross-Tsur, Shalev, Manor, & Amir, 1995; Rapin & Allen, 1988; Weintraub & Mesulam, 1983).

Despite decades of research, the etiology of spelling and reading failure are still debated. It is now well established that dyslexia underlies a neurological disorder with a genetic origin (Galaburda, LoTurco, Ramus, Fitch, & Rosen, 2006). However, the neuronal dysfunctions are still being unraveled. Clinical data proposed three different subtypes: phonological, surface and mixed (Castles & Coltheart, 1993). Individuals with phonological dyslexia show a deficiency in the development of graphophonemic reading procedures and have difficulties in reading pseudowords or newly encountered words. Surface dyslexics show problems with the development of lexical procedures, which is crucial to reading irregular words.

Other dyslexia categories were proposed in line with pathopyhsiological hypotheses and to the different symptoms dyslexics are affected with. The variety of symptoms is consistently related to reading problems and phonological difficulties (the mental representation and processing of speech sounds). Additionally, dyslexic individuals exhibited sensory disorders in the visual, auditory and tactile domains as well as problems in balance and motor control (Ramus, 2003; Stein et al., 1997). It has been suggested that one third of dyslexic individuals suffer from auditory deficit, another third from visual impairments and the remaining third from a motor disorder. It is also conceivable that sensory or motor deficits manifest in reading disorders. A few studies pointed to a partial, but not a total, overlap across deficits in the different domains (Ramus et al., 2003c).

Several theories exist (see Figure 1) which focus on the general auditory (Baldeweg et al., 1999; Farmer et al., 1995; Reed, 1989; Tallal, 1980), visual (Livingstone et al., 1988; Lovegrove et al., 1980; Stein et al., 1997) or motor impairments (Nicolson et al., 1990; Rudel, 1985; Wolff et al., 1990) dyslexic individuals often suffer from. The most accepted theory is the phonological processing deficit hypothesis (Bradley et al., 1983; Ramus et al., 2003b). Difficulties with the neural representation of the phonological structure of speech has been observed across languages (Goswami et al., 2010).

2 The Cognitive and Behavioral Level of Developmental Dyslexia

2.1 The Phonological Deficit Theory

The phonological deficit theory postulates a specific impairment in the representation, storage and/or retrieval of speech sounds (Bradley et al., 1983; Ramus et al., 2003b) as well as a reduced development of an appreciation for the segmental nature of speech (Frith, 1985). Once the child realizes that spoken words are composed of smaller segments, namely the phonemes, the learning of the phoneme to grapheme mapping is enabled. Graphemes and phonemes are the basic elements of correspondence between written and spoken language, in an alphabetic language. Alphabetic languages vary in their regularity of the phoneme to grapheme correspondence. The acquisition of this culturally defined letter and speech sound knowledge is a critical and fundamental skill for learning to read and spell (Bryne, 1998; Byrne, 1998; Muter, Hulme, Snowling, & Stevenson, 2004). As learning to read requires mastery of phoneme to grapheme mapping, learning speed generally relates to the consistency of orthographies. Less consistent orthographies such as English, require of readers a relatively longer period of training to acquire literacy, as compared to shallow orthographies such as Italian or Spanish (Gabrieli, 2009). However, difficulties with the neural representation of the phonological structure of speech have been observed across languages (Goswami et al., 2010).

Extended practice of symbol-sound learning leads to improved word recognition (Li, Shu, McBride-Chang, Liu, & Xue, 2009). Due to the fact that symbol-sound learning is essential for word decoding, reading skills have been linked with paired associative learning, i.e. the ability to associate a verbal and visual stimulus with each other (Hulme, Goetz, Gooch, Adams, & Snowling, 2007). In literate adults, the phoneme to grapheme mapping occurs rapidly and automatically (Paulesu et al., 1996) and can be considered an over-learned, paired association process (van Atteveldt, Formisano, Goebel, & Blomert, 2007b). Notably, dyslexics often have extreme difficulties in learning the letter-sound correspondence and a high level of these culturally defined association may never be reached (Vellutino, Fletcher, Snowling, & Scanlon, 2004).

DD was identified as a problem of processing phonological information. For example dyslexics compared to non-dyslexics showed less sensitivity to rhyme (Bradley et al., 1983), subtle differences between phonemes that are acoustically similar to each other or a categorical perception deficit. The categorical perception deficit was revealed when children had to categorize an artificial acoustic continuum between the two syllables “ba” and “da”, in stimuli si-

tuated in close to inter-categorical boundaries, such as articulatory oppositions “ba”-“da”; “da”-“ga”; or less often for voice onset oppositions such as “ba”-“pa” (Manis et al., 1997). Although the nature of the phonological problems is still debated (Ramus et al., 2003c), three main dimensions of the phonological deficit have been postulated: poor phonological awareness (the ability to identify or manipulate sounds within words) (Bradley et al., 1983; Liberman, Shankweiler, Fischer, & Carter, 1974; Manis, Custodio, & Szeszulski, 1993), poor phonological memory (the short-term retention of speech-based information) (Bowers & Swanson, 1991; Wolf, 1986) and slow lexical retrieval (evidenced in rapid serial naming tasks) (Snowling, Bishop, & Stothard, 2000b). All three phonological skills in turn involve a whole network of cortical areas (Turkeltaub, Gareau, Flowers, Zeffiro, & Eden, 2003).

The Phonological Awareness

Phonological awareness is the ability to identify and manipulate the sound structure of words (Snow, Burns, & Griffin, 1998; Snowling, 1987) and is the most accurate predictor of later reading and spelling acquisition (Siok & Flechter, 2001). Deficits in phonological awareness lead to the poor development of word recognition (Liberman, 1998) and causes particular problems in print related decoding tasks such as pseudoword reading. Pseudoword reading problems, therefore, reflects genuine deficits rather than just delays in reading skill acquisition (Savage & Frederickson, 2006). Training and practice with reading pseudowords improves the phonological awareness (Liberman, 1998) and therefore the reading acquisition across languages (Stainthorp & Hughes, 1998). Additionally, phonological awareness is required for rhyming tasks and counting syllables (Temple et al., 2003).

The Phonological and Verbal Memory

There is evidence that dyslexic children show weak memory performance in phonological processing yet show intact or typical visuo-spatial memory skills (Everatt, Jeffries, Elbeheri, Smythe, & Veii, 2006). In recognition memory tasks, studies have found differences in word processing between dyslexic adults and non-impaired readers (Russeler, Probst, Johannes, & Munte, 2003). However, dyslexic children are not generally impaired in recognition memory. Dyslexic children vs. non-dyslexic children performed similarly in recognizing graphic material but showed impairments specific for linguistic material like words (Schulte-Korne, Deimel, Bartling, & Remschmidt, 2004b). Poor verbal short-term memory span in DD is reported extensively (Helland & Asbjornsen, 2004; Jorm, 1983; Mann, Liberman, & Shankweiler, 1980). Short-term memory impairments occurr especially with long words, which leads to the suggestion that tasks for verbal material require inner speech and phonological storage

(Paulesu et al., 1996). Generally, it is still being unraveled whether the short term memory impairment is caused by phonological loop problems or a more basic deficit in phonological processing, because it is difficult to distinguish phonological memory from other phonological processes (Snowling, Chiat, & Hulme, 1991). This induced some controversy in the research field over the relative contribution of phonological and memory processes in dyslexia (Gathercole, Willis, & Baddeley, 1991; Snowling et al., 1991). However, there is also converging evidence for a central executive deficit in the case of dyslexia (Asbjornsen & Bryden, 1998; de Jong, 1998; Gathercole, Pickering, Hall, & Peaker, 2001; Helland & Asbjornsen, 2000; Reiter, Tucha, & Lange, 2005), indicating that poor performance on working memory tasks might not emerge from a phonological deficit alone. An executive deficit might be related to impaired activations in dorsolateral prefrontal and parietal cortices, whereas a phonological deficit might be associated with inferior frontal and superior temporal brain areas (Beneventi, Tonnessen, Ersland, & Hugdahl).

The Rapid Automatic Naming

The rapid automatic naming (RAN) theory claims that dyslexic individuals suffer, (beyond phonological processing problems), from deficits in the automatisation of word learning (Manis, Doi, & Bhadha, 2000). It is assumed that rate-limiting factors underlie both speeded naming and the quality and accessibility of orthographic representations in the lexicon during reading acquisition. Thus, poor readers show particular difficulties in tasks requiring speeds and serial access to – and retrieval of – verbal labels for visually presented stimuli (Logan, 1988). RAN has been considered as a language skill that is part of a broad family of phonological tasks (Torgesen, Wagner, Rashotte, Burgess, & Hecht, 1997). There were RAN differences between dyslexic and non-dyslexic individuals for digits yet none revealed for pictures. These results suggest that naming effects in reading and spelling are quite specific to alphanumeric stimuli. Therefore it has been concluded that alphanumeric RAN may be particularly strongly associated with attainment in spelling, and possibly of comparable importance to phonological processing (Savage et al., 2006).

Counterarguments

The phonological deficit theory has been criticized because it is not able to explain the occurrence of aural, visual and motor disorders in dyslexic individuals. The providers of this theory dismiss these disorders and consider their co-occurrence with the phonological deficits as potential markers of DD, but do not consider them as playing a casual role in the etiology of reading and spelling impairment (Snowling et al., 2000b). Detractors of the phonological

processing theory point to reports of children and adults with brain damage, who have difficulties in non-word reading but nevertheless exhibit good phonological awareness. They concluded that such evidence should question the causal link between a phonological deficit and dyslexia. Additionally, it has been argued that phonological representations themselves have been demonstrated to be normal in DD, but a task specific deficit might occur in the access to such representations (Vidyasagar & Pammer, 2010).

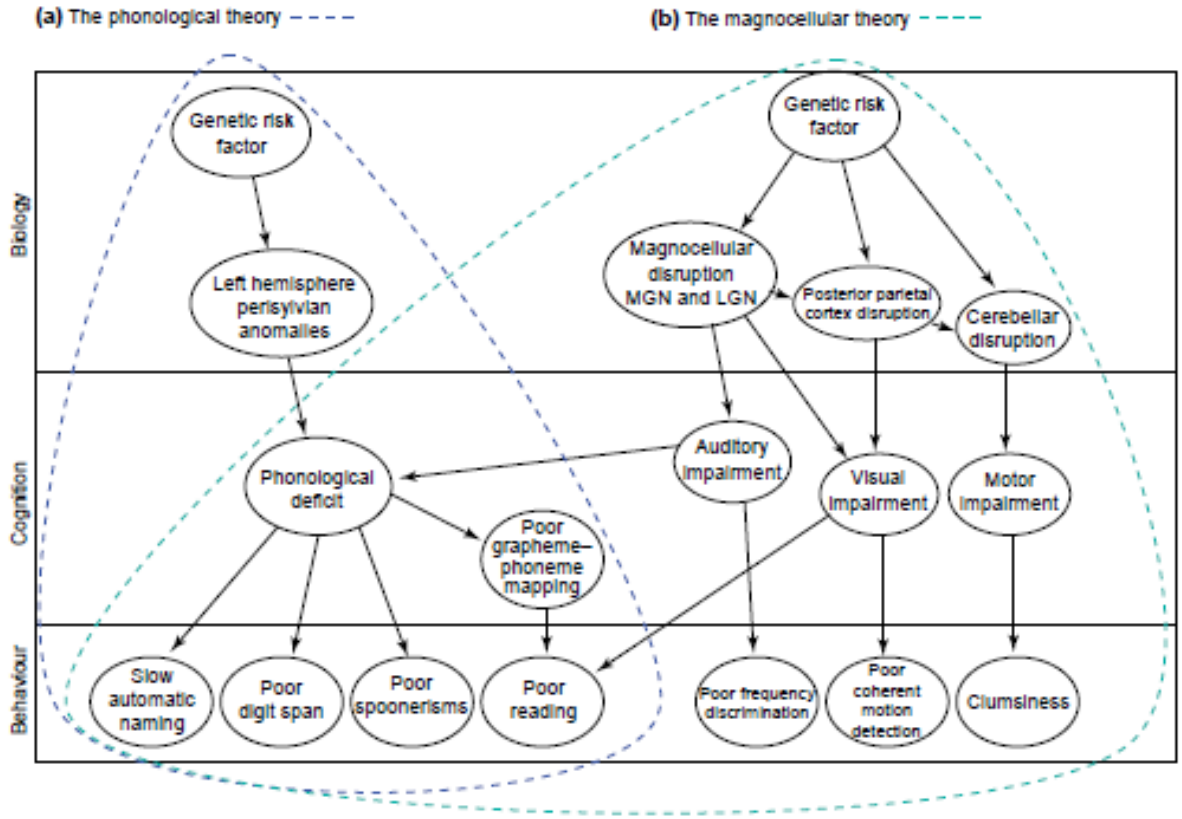

Figure 1 depicts the main theories trying to explain the etiology of DD. They are: (a) the phonological theory and the (b) magnocellular theory. There are traits at the biological, cognitive and behavioral level represented. Both theories agree that DD underlies a genetic origin causing neuronal abbreviations. However, the phonological deficit theory assumes that anomalies in the perisylvian regions are responsible for the phonological processing deficit and in turn for the poor phoneme to grapheme mapping. In contrast, the magnocellular theory suggests that impairments in the magnocuellular system cause sensory (i.e. aural and visual) as well as motor impairments. This theory assumes that impairments in the auditory system are responsible for the phonological deficit (Ramus, 2004).

2.2 The Magnocellular Theory

The magnocellular theory agrees with the phonological deficit, but considers a more basic auditory and visual impairment as well as sensorimotor deficit. This theory postulates that the magocellular dysfunctions that might cause phonological deficits are not only restricted to the visual system but generalized for all modalities: visual, auditory, tactile and motor (for attentional variant see (Hari & Renvall, 2001; Vidyasagar et al., 2010)). The magnocellular system

is responsible for timing events when reading. Due to the fact that the cerebellum is the head ganglion of the magnocellular systems, it contributes to binocular fixation and to inner speech sounding of words (Stein et al., 1997). Evidence especially relevant to the magnocellurar theory includes magnocelluar abnormalities in the medial and lateral geniculate nucleus of dyslexics' brains (Galaburda, Menard, & Rosen, 1994; Livingstone, Rosen, Drislane, & Galaburda, 1991). This leads to poor performance of dyslexic individuals in the tactile domain (Grant, Zangaladze, Thiagarajah, & Sathian, 1999; Stoodley, Talcott, Carter, Witton, & Stein, 2000) and the co-occurance of visual and aural difficulties in some dyslexics (Cestnick, 2001; Van Ingelghem et al., 2001; Witton et al., 1998). The impaired development of magnocells is caused by a genetic origin. This is associated with the region of the Major Histocompbility Complex (MHC) Class 1 on the short arm of chromosome 6. This region helps to control the production of antibodies. These antibodies are proposed to impair the development of magnocells (Stein, 2001).

Counterarguments

The counter arguments of the magnocellular theory are that it only partly succeeds in explaining the whole dataset. It fails particularly to explain why the prevalence of sensorimotor dysfunctions is so much lower than that of the phonological deficit in dyslexic individuals. The causal relationship between reading impairments and sensory and/or motor disorders is not clear (Ramus, 2003; Rosen, 2003).

2.2.1 The Auditory Processing Deficit

The impairments in phonological processing (the use of the sound structure of language) especially affect the ability to properly map the orthographic code to the phonological code. It has been suggested that the deficit in phonological processing originates from an elementary general difficulty in decoding acoustic information with certain temporal properties (Baldeweg et al., 1999; Tallal, 1980). The characterization of the aural dysfunctions is consistent with the magnocellular theory, because magno-cells are particularly sensitive to high temporal frequencies (Stein, 2001). The empirical evidence for the auditory temporal hypothesis was investigated across a wide range of auditory tasks. These ranged from classical temporal order judgment (Baldeweg et al., 1999; Tallal, 1980) and repetition tests (De Martino, Espesser, Rey, & Habib, 2001; Rey, De Martino, Espesser, & Habib, 2002), to discriminating of frequency and intensity (Amitay, Ahissar, & Nelken, 2002a; Amitay, Ben-Yehudah, Banai, & Ahissar, 2002b; France et al., 2002) as well as several detection tasks such as gaps (Van In-

gelghem et al., 2001), illusory movement (Kronbichler, Hutzler, & Wimmer, 2002) and frequency to amplitude modulation (Goswami et al., 2002; Witton, Stein, Stoodley, Rosner, & Talcott, 2002). Additionally, there were categorical perceptions of phonemes and non-speech analogues (Breier et al., 2001; Serniclaes, Sprenger-Charolles, Carre, & Demonet, 2001) and backward masking tasks applied (Ramus et al., 2003c; Rosen & Manganari, 2001).
Dyslexic individuals showed difficulties discriminating rhythm and/or pitch (Baldeweg et al., 1999; Kujala et al., 2000) as well as in discriminating and sequencing pairs of short-lived stimuli with short inter stimulus interval (ISI). The impairment of processing stop consonants by short and rapid spectral changes was interpreted as a temporal processing deficit for speech perception in dyslexic individuals (Cornelissen, Hansen, Bradley, & Stein, 1996; Manis et al., 1997). The failure to correctly represent short sounds and fast transitions indicate that dyslexics have difficulties with all aspects of temporal analysis. These findings lead to the suggestion that dyslexics might have difficulties with acoustic temporal pattern perception, which might stem from a more primary perceptional deficit. The perceptual deficit might affect the rate and accuracy of processing information. It has been concluded that the dyslexic deficit was specific to the processing of brief stimuli that occurs in rapid succession. This theory is called the “rapid” or “temporal” auditory processing deficit (Tallal, 1980). Beyond focusing on the rapid changes in frequency and intensity that characterize formants (Tallal, 2004), the importance of the slower amplitude modulations in the speech stream for speech perception has been recognized. Auditory science could also demonstrate that selectively degrading modulation frequencies near the syllabic rate (4-16 Hz) degrades volunteers’ ability to identify consonants and to understand sentences (Drullman, Festen, & Plomp, 1994).
It was investigated whether or not early difficulties in perceiving auditory sensory cues, speech rhythms, and prosody could lead developmentally to impairments in phonology. This was examined in a sample of English, Spanish or Chinese speaking children with and without dyslexia. The data established rise time discrimination (critical for the rhythmic timing of speech) as a universal cross-language sensory deficit in DD. The finding revealed that the rise time sensitivity was a significant predictor of phonological awareness. It is the only known consistent predictor of reading acquisition (Goswami et al., 2010).

Counterarguments

A line of criticism focuses on inconsistent results between data and the theory (Ramus, 2001). There were some aural deficits found in tasks that do not tap rapid auditory processing, such as frequency discrimination (Amitay et al., 2002b; France et al., 2002) or frequency modulation detection at 2 Hz (Witton et al., 2002). On the other hand, rapid auditory processing

seemed often to be intact, especially when inter-stimulus intervals were manipulated in a systematic manner (Amitay et al., 2002b; France et al., 2002). The auditory processing disorders are restricted to a subset of the dyslexic population and have little influence of the development of phonology and reading. It has been argued that the occurring phonological deficit can arise in absence of any auditory disorder (Ramus et al., 2003c) and that the auditory deficits do not predict the phonological deficits (Marshall, Snowling, & Bailey, 2001; Rosen et al., 2001).

2.2.2 The Visual Processing Deficit

Providers of the visual processing deficit postulate that the phonological problems and the reading impairment both arise by way of a basic visual-processing deficit (i.e. poor visual/ orthographic coding) (Stein et al., 1997). Visual perception deficits have been observed in dyslexics for a variety tasks: spatial (such as contrast) (Stein, 2001; Stein et al., 1997), positional, and temporal (such as motion discrimination) tasks (Hill & Raymond, 2002). Dyslexics yielded low motion sensitivity, poor visual localization (particularly of the left side; left neglect) (Livingstone et al., 1988), unsteady binocular fixation, low flicker sensitivity (Martin & Lovegrove, 1987) and reduced pre-attentive selection of features in space (Vidyasagar, 1999). These functions are controlled by the dorsal pathway which receives input from mangocellular cells. The magnocellular pathway arises from cells widely distributed across the retina and projects via the ventral lateral geniculate nucleus (LGN) to the visual cortex, and thereafter to the parietal cortex. The ventral pathway is sensitive to qualities such as color, texture and form (Livingstone et al., 1988) as well as to high spatial frequencies (Bundo et al., 2000). The ventral stream has moderate temporal resolution and is controlled by the parvocellular system, which originates in cells concentrated in the fovea and projects via the dorsal LGN to the visual cortex and then mainly to the temporal cortex.

Vision-related research of dyslexia has focused on functions associated either with the transient visual system or the magnocellular pathway (Skottun, 2000). The magnocellular system is responsible for high motion sensitivity and for the control of the eye movement. Thus, the dysfunctional magnocellular pathway might destabilize the binocular fixation. Letters might then appear to move around and cause visual confusion. Dyslexics show often poor binocular control and unsteady eyes while reading. Due to unstable vision they make some reading errors (Cornelissen, Bradley, Fowler, & Stein, 1991). Additionally, evidence exists demonstrating that the magnocellular system is also an important for subserving visual attention (Stein,

2001). It has been argued that the attentional mechanism controlled by the dorsal pathway helps in the serial scanning of letters, and that any deficits in this process will cause a cascade of effects, including impairments in the visual processing of graphemes and their translation into phonemes (Vidyasagar et al., 2010).

Counterarguments

The visual side of the magnocellular theory has been criticized due to failures to replicate the findings of a visual deficit (Johannes, Kussmaul, Munte, & Mangun, 1996; Victor, Conte, Burton, & Nass, 1993). The visual deficits seem to be restricted to a subset of dyslexics (Amitay et al., 2002b; Cornelissen, Richardson, Mason, Fowler, & Stein, 1995; Witton et al., 1998). Additionally, the visual impairments, when found, were observed across a whole range of stimuli, not just those uniquely tapping the magnocellular system (Amitay et al., 2002b; Skottun, 2000). The missing correlation between visible persistence and spelling, phoneme awareness or speech discrimination indicated that neither the magnocellular nor the parvocellular system cause the deficit dyslexics are affected from (Schulte-Korne, Bartling, Deimel, & Remschmidt, 2004a).

2.2.3 The Motor Control Syndrome

The framework of cerebellar deficit theory claims that DD is associated with the problem of acquiring and automating reading and spelling due to cerebellar dysfunctions (Nicolson, Fawcett, & Dean, 1995). It has been suggested that the automaticity deficit results beside problems in learning literacy also in impairments in other domains, such as phonology, motor skills for speech production (Rudel, 1985; Wolff et al., 1990) and speed of information processing (Fawcett & Nicolson, 2007). Automation is, for the most part, controlled by the cerebellum (Brindley, 1964; Ito, 1984). The cerebellum has links to pre-motor and prefrontal areas, including Broca's language area. Hence it has a crucial role in linguistic and cognitive skills such as the speed and fluency of information processing (Nicolson & Fawcett, 1994). Additionally, it is well established that the cerebellum plays an important role in motor functions and coordination (Ito, 1993; Leiner, Leiner, & Dow, 1989, 1993). Imaging studies have confirmed the involvement of the cerebellum in reading (Fulbright et al., 1999; Turkeltaub, Eden, Jones, & Zeffiro, 2002). In addition to automation and language problems, dyslexics demonstrate, while engaged in attention-demanding circumstances, difficulties in implicit learning, time estimation, eye blinking, motor-coordination, and automatic balance (Nicolson et al., 1990). This observation suggests that motor tasks in these children are undertaken at the

expense of attentional resources. Proponents of the cerebellar dysfunction theory suggest that pathological cerebellar activation is present from birth and causes difficulties in the acquisition and the automatition of elementary articulatory and auditory skills, which in turn causes difficulties in phonological processing, together with visual skills such as eye movement and letter recognition. These disorders were suggested to cause the early problems in learning to read and spell (Nicolson et al., 1999).

Counterarguments

Criticism has been raised because independent studies could not replicate the deficits, notably those in implicit learning (Russeler, Gerth, & Munte, 2006), automaticity and time estimation (Ramus et al., 2003c). It has been argued that motor impairments are restricted to a subset (estimated between 30 to 50%) of the dyslexic individuals (Ramus, Pidgeon, & Frith, 2003a; Ramus et al., 2003c). Additionally, there is little evidence for a causal link between motor difficulties and phonological processing, and /or reading (Ramus et al., 2003a). Moreover, the theory fails to explain the sensory disorders. Critics have argued whether the apparent lack of use of the cerebellum truly reflects a cerebellar abnormality rather than abnormal magnocellular function or abnormal connectivity (Bishop, 2002; Zeffiro & Eden, 2001).

3 The Biological Origin of Developmental Dyslexia

3.1 The Genetic Basis

A postulate in much of current research in the field of DD is that the difficulties occurring on the cognitive and behavioral level are related to constitutional characteristics of the brain due to genetic origins. The genetic origin was suggested because a high familial occurrence was observed (Cardon et al., 1994; Olson, Wise, Conners, Rack, & Fulker, 1989; Stevenson, Graham, Fredman, & McLoughlin, 1987). Hence, a strong heritability (54-75%) was proposed, with a higher concordance rate for monozygotic (84-100%) compared to dizygotic twins (20-35%). It has been postulated that inheritance is autosomal dominant (Hallgren, 1950). Different chromosomes and genes have been implicated for various aspects of reading disorders.
It was suggested that chromosome 15 is related to performances of single word reading, while chromosome 6 would be related to phonological awareness (Grigorenko et al., 1997). Additional chromosomes such as 1, 2, 3, and 18 were reported to affect reading difficulties (Demonet, Taylor, & Chaix, 2004). There is evidence that 10 susceptible genes in DD are responsible for subtle cortical malformations involving neural migration and axon growth. This leads to abnormal cortico-cortical and cotioco-thalamic circuits that affect sensorimotor, perceptual and cognitive processes critical for reading (Cope et al., 2005; Hannula-Jouppi et al., 2005; Poelmans et al., 2009).
In the present state of knowledge, the associations between the genetic and phenotypic forms of DD are still unclear. It would be most prudent to claim that the variety of behavioral deficits in DD have a common underlying genetic and brain development cause. Any causal relationships among perceptual and linguistic deficits will need underpinnings by appropriate, developmentally designed human studies. For instance, a challenge will be to demonstrate how variant gene functions affect brain development. Genes can result in exquisitely focal, anatomical, and behavioral phenotypes, and genes can cause the anatomical anomalies and behavioral deficits in dyslexia (Galaburda et al., 2006).

3.2 The Neuronal Basis

Anatomical Anomalies

Anatomical findings in post-mortem as well as in vivo imaging studies documented distinctive architectural features in dyslexics compared to non-dyslexic individuals. The most signif-

icant contribution to the neurology of DD was the disclosure of subtle cortical neuronal migration anomalies, observed in post-mortem brains. These included ectopias (small neuronal congregations located in an anormal superficial layer) which were distributed across both frontal regions, in the left language areas. Dysplasia has also been observed in form of loss of characteristic architectural organization of the cortical neurons, mainly subjacent to the site of ectobipas. More rarely, vascular micro-malformations were found (Galaburda & Kemper, 1979; Galaburda, Sherman, Rosen, Aboitiz, & Geschwind, 1985; Kaufmann & Galaburda, 1989). Dyslexic brains often exhibit abnormal ectopias and microgyrias all over the cerebral cortex and especially in the temporo-parietal association areas over perisylvian regions (Galaburda et al., 1985). It has been suggested that cortical abnormities in the left perisylvian areas could cause the phonological and perhaps various cognitive deficits (Brunswick, McCrory, Price, Frith, & Frith, 1999; Paulesu et al., 1996; Pugh et al., 2000b; Shaywitz et al., 2002). Additionally, cytoarchitectonic anomalies in dyslexic individuals were observed in the thalamus, such as in the medial (MGN) of the auditory (Galaburda et al., 1994) and the lateral geniculate nucleus (LGN) of the visual pathway (Livingstone et al., 1991). These magnocellular layers were more disorganized and contained on average 27% smaller bodies. This might cause visual and auditory deficits or disorders in all sensory modalities (Nicolson et al., 1999; Skottun, 2000; Stein, 2001; Stein et al., 1997; Tallal, 1980).

In addition to the various microscopic malformations, macroscopic peculiarities were also found. One striking anatomical finding is that the normal asymmetry of the planum temporale (PT) favoring the left hemisphere tends to be absent in dyslexic individuals (Galaburda, LeMay, Kemper, & Geschwind, 1978). In dyslexic postmortem brains, symmetrically sized PTs (i.e. an enlargement of the right hemisphere PT) were found (Galaburda et al., 1985; Humphreys, Kaufmann, & Galaburda, 1990). Contrarily, in non-impaired individuals, the PT was more likely to be larger in the left than the right hemisphere (Geschwind & Levitsky, 1968). The PT is a triangular landmark situated on the supra-temporal surface, posterior to the Heschl's gyrus, inside the Sylvian fissure, and is part of the cortical language network. The left PT has been proposed as an important index for the left hemispheric language lateralization (Galaburda, 1993; Shapleske, Rossell, Woodruff, & David, 1999). Some data evidence that non-leftward PT asymmetry is associated with deficits in verbal comprehension, phonological decoding, and expressive language. Dyslexics with symmetric PTs exhibited pure phonological deficits in reading (Larsen, Hoien, Lundberg, & Odegaard, 1990). Furthermore, there have been significant correlations ($r= 0.69$, $p=0.005$) between scores in comprehension tests and the posterior superior surface of the temporal lobe asymmetry as reported in dyslex-

ics (i.e. those with higher scores had more leftward asymmetry). This indicates that the direction of the superior surface of the temporal lobe asymmetry might serve as a risk factor for reading comprehension problems (Kushch et al., 1993). These findings might indicate the possible neuroanatomical basis of linguistic processing symptoms characterized as DD. However, it is important to note that the PT symmetry in DD could not always be replicated by post-mortem brain analysis (Livingstone et al., 1991) or MRI (Heiervang et al., 2000).
In German dyslexic adults, reduced gray matter volume in the bilateral superior temporal gyrus (Steinbrink et al., 2008), in the bilateral fusiform gyrus, the bilateral anterior cerebellum and the right supramarginal gyrus has been identified (Paulesu et al., 2001; Ramus, 2004; Steinbrink et al., 2008). Other anatomical structure differences in DD brains have been suggested, such as in the pars triangularis and the cerebellum (Middleton & Strick, 1997; Schmahmann & Pandya, 1997). In Italian dyslexic adults, smaller gray matter volumes in the right posterior parietal lobule, the precuneus, and the right SMA were found (Menghini et al., 2008). Abnormal symmetry in the posterior parietal cortex of dyslexic brain was also revealed by (Galaburda et al., 1978). Generally, in dyslexics, a widespread disruption of the normal connection is found. Also notable is that the corpus callosum was observed to be more rounded with an evenly thicker callosal shape (Robichon & Habib, 1998).
In conclusion, studies revealed reduced or increased gray matter density or volume in the specific regions of dyslexic brain (i.e. left- and right-temporal structures, bilateral parts of the cerebellum, bilaterally in the precentral gyrus, and in the left posterior middle temporal gyrus. The reduction of gray matter might reflect regional decrease of neurons, which in turn results in reading impairments.

Diffusion Tensor Imaging

Diffusion tensor imaging (DTI) offers in-vivo information on the integrity of white matter structures (anisotrophy) and connectivity (fiber tracking) in the human brain. DTI provides reproducible quantitative measures, such as mean diffusivity and fractional anisotrophy (FA). FA has been shown to be sensitive to individual differences in WM integrity and to disease conditions that lead to loss of WM integrity (Lim & Helpern, 2002; Mukherjee et al., 2000). There have been positive associations between lower asniosotrophy coherence in the left temporo-parietal network and performance scores in children (n=14), with a wide range of reading performance levels revealed. This finding supported the notion that the structure of the left temporo-parietal neural network pathways was a significant component of the neural system needed to develop fluent reading (Deutsch et al., 2005). The strong correlation between FA

values in the left temporo-parietal white matter (WM) region and standardized reading scores of typically developing children could be replicated by (Niogi & McCandliss, 2006). Dyslexic adults who reported reading difficulty as children exhibited decreased diffusion aniosotrphy bilaterally in temporo-parietally WM (Klingberg et al., 2000). White-matter organization appears to be weaker in the left posterior brain region in dyslexic compared to non-dyslexic individuals (Gabrieli, 2009). These results indicate that the disruption of WM could relate directly to the disruption of dynamic sensory processing that has been observed in dyslexia. FA might reflect the microstructure of WM tracts that may contribute to reading ability by determine the strength of communication between cortical areas involved in visual, auditory, and language processing (Caylak, 2009).

Additionally, significant correlations between performance on working memory task and frontal WM tract regions were found in children with dyslexia (Niogi et al., 2006). Fronto-striatal differences in FA were associated with measures of cognitive control (Nagy, Westerberg, & Klingberg, 2004; Olesen, Nagy, Westerberg, & Klingberg, 2003). It has been suggested that severity of cognitive impairment due to closed head brain injury may correlate with severity of damage to white matter integrity (Mathias et al., 2004).

Taken together, particular regions of WM tracts are specifically associated with individual differences in separable domains of cognitive function. The relation between individual differences in specific domains of cognitive performance, such as reading and working memory, are likely mediated by individual microstructure differences in specific WM tract circuitry by (Niogi et al., 2006). Dyslexic adults who reported reading difficulties as children exhibited decreased diffusion aniosotrphy bilaterally, in temporo-parietally WM (Klingberg et al., 2000). WM organization appears to be weaker in the left posterior brain region of dyslexics, compared to non-dyslexic individuals (Gabrieli, 2009). These results indicate that the disruption of WM could relate directly to the disruption of the dynamic sensory processing that has been observed in dyslexia. FA might reflect the microstructure of WM tracts, which in turn may contribute to reading ability by determining the strength of communication between cortical areas involved in visual, auditory, and language processing (Caylak, 2009).

Additionally, children with dyslexia showed significant correlations between working memory task performance and frontal WM tract regions (Niogi et al., 2006). Fronto-striatal differences in FA were associated with measures of cognitive control (Nagy et al., 2004; Olesen et al., 2003). It has been suggested that the severity of cognitive impairment, due to closed head brain injury, may correlate with severity of damage to white matter integrity (Mathias et al., 2004).

Taken together, particular regions of WM tracts are specifically associated with individual differences in separable domains of cognitive function. The relation between individual differences in specific domains of cognitive performance, such as reading and working memory, are likely mediated by individual microstructure differences in specific WM tract circuitry (Niogi et al., 2006).

3.3 The Functional Manifestations

The Findings of fMRI Data

Results from functional imagine studies evidence a different activation pattern for dyslexic compared to non-dyslexic individuals. Notably, the normal development of reading skills occurs across an extended period of time during childhood. This indicates that different cortical areas differ over the course of reading acquisition. However, skilled adult readers activate a widely distributed network, dominated by the left hemisphere with two posterior pathways for visual and orthographic information (Pugh et al., 2000a). One stream is the ventral or lexical pathway that spreads along the ventral lobe from the posterior to the anterior regions (Pammer et al., 2004). In the left occipitootmporal/fusiform regions, with extension into the middle and inferior temporal gyri, a fast visual word processing system was localized by (Sandak et al., 2004). Other authors proposed a more specific region and localized the visual word form area (VWFA) in the left mid-fusiform gyrus (Cohen et al., 2000; Cohen et al., 2002; Dehaene, Le Clec, Poline, Le Bihan, & Cohen, 2002) and thus claimed that this area is progressively recruited for fast visual letter and word recognitions in the course of reading. The VWFA has also been considered as a critical component of the mature reading network (Brem et al., 2010). Due to the fact that reading is a recent cultural intervention, it is plausible that some visual processing elements (Dehaene, Cohen, Sigman, & Vinckier, 2005) adopt additional functions and, through practice, are increasingly sensitized to print processing (Brem et al., 2010). After sound-based word recognition skills become more automatic and fluent, the occipito-temporal cortex becomes increasingly involved and it is possible that the direct visual access to the mental lexicon becomes the predominant reading strategy (Pugh et al., 2000a; Shaywitz et al., 2002). However, to date it has still not yet been unraveled how the VWFA functions integrate phonology and orthography.

Measurements of dyslexic individuals showed reduced neuronal activities over leftward occipito-temporal regions during letter-string perception (Helenius, Tarkiainen, Cornelissen, Hansen, & Salmelin, 1999; Paulesu et al., 2001; Salmelin & Helenius, 2004)

as well as during different reading tasks (Meyler et al., 2007; Paulesu et al., 2001; Shaywitz et al., 2002). The correlation of the activation in the left occipito-temporal cortex with reading performance could be evidenced in both typically developing and reading impaired children (Shaywitz et al., 2002). This left hemispheric processing dominance for word decoding is enhanced in skilled readers (McCandliss et al., 2003b). In kindergarten, children with no knowledge for the grapheme to phoneme correspondence were given eight weeks of training (totalling 3.6h) of sound-letter associations. An increase to print sensitivity was found in two clusters on the left and right occipito-temporal lobes (fusiform gyrus and inferior temporal gyrus) as well as in the cuneus (Brem et al., 2010). This finding indicates that neuronal reorganization over occipito-temporal brain areas occurs, and underlies notions relating the specific practice of phoneme to grapheme mapping and the neuronal reorganization required for acquiring reading skills. These neuronal reorganizations might reflect processes of automated reading.

The second posterior pathway is the dorsal stream, or the "sensory-motor" integration pathway, which runs through the temporal-parietal junction and further to the moor prefrontal areas, particularly Broca's area. This stream is dominated by magnocellular neurons specialized for detecting visual motion as well as controlling eye and limb movements (Stein, 2001; Stein et al., 1997) and projects from occipital regions into the angular gyrus (AG) and supramargnial gyrus (SMG) in the inferior parietal lobule (IPL) (Price, 2000). The AG and SMG have generally been considered to serve as a mediator, relating the output from orthographic processing at extra striate regions (e.g. the lingual gyrus) to lexical and linguistic representations (Geschwind, 1965). It therefore plays a pivotal role in phonological decoding (mapping print to sound) at the word level (Damasio & Damasio, 1983). Thus, the left temporo-parietal region is hypothesized to provide cross-modal relation of auditory and visual processes during reading (Gabrieli, 2009) as well as integrating the word forms with their semantic representation (Booth et al., 2003). Additionally, it has been suggested that this region may function as a sound-based medium for storing and integrating phonological, semantic and syntactic information in verbal working memory (Keller, Carpenter, & Just, 2001).

Dyslexic adults (Eden et al., 2004; Rumsey et al., 1999) and dyslexic children (Aylward et al., 2003) exhibited reduced activation in the left parietal region when reading tasks on word-level. Additionally, reduced bilateral parietal hemodynamic responses were found in children reading sentences (Meyler, Keller, Cherkassky, Gabrieli, & Just, 2008).

Furthermore, decreased neuronal activation in parietal regions were observed in dyslexics compared to non-dyslexic individuals for tasks demanding phonological awareness (e.g.

rhyming tasks) (Paulesu et al., 1996; Rumsey et al., 1992), pronunciation and decision making tasks (Rumsey et al., 1997a) and hierarchically organized tasks with phonological process (Shaywitz et al., 1998). Correlating the phonological ability and activation of the left perisylvian region in typically developing children led to the suggestion that cortical activation patterns related to those with reading impairment and may represent points of increasing severity on a continuum that includes individual differences in the typical range of performance (Turkeltaub et al., 2003). However, left temporo-parietal regions (middle temporal cortex and the AG) were also involved in semantic or sentence verification tasks (Meyler et al., 2007; Shaywitz et al., 1998). During semantic word matching, decreased activations in the left occipto-temporal cortex, left middle temporal cortex, the left angular gyrus as well as the left middle frontal gyrus was observed for both English and Chinese dyslexic individuals (Hu et al., 2010). During a phonological judgment task (tone pairs were the same or not) dyslexic vs. non-dyslexic children had more hemodynamic activity in the right than left inferior temporal gyrus and in left precentral gyrus, as well as in the left orbital frontal cortex. During phonological judgements, less neuronal activity was yielded, for dyslexics compared to non-dyslexics, in bilateral middle frontal gyrus. A reduced hemodynamic response was found in dyslexic compared to non-dyslexic children in the left insula and the left inferior temporal gyrus. These results indicate that dyslexic children also differ in auditory language processing skills that do not require reading (Corina et al., 2001).

An anterior component, which is connected to the two posterior pathways (Price, Warburton, Moore, Frackowiak, & Friston, 2001), is implicated to play a pivotal role in phonological and articulatory aspects as well as to serving as an important function in silent reading and naming (Fiez & Petersen, 1998; Frackowiak et al., 2004).

In this anterior system, and more precisely in the inferior frontal gyrus, activations revealed by dyslexics were atypical. During a silent reading task of German words and pronounceable non-words, dyslexics showed (compared to non-dyslexic children) reduced hemodynamic responses in the left inferior frontal gyrus (Georgiewa et al., 2002). Significant group differences between dyslexic and non-dyslexic children were also examined in Broca's area and the left inferior temporal region for both, non-word reading and the phonological transformation tasks. In the previously mentioned study, the participants had to perform four different tasks: 1) passive viewing of letter strings (control condition), 2) passive reading of non-words, 3) passive reading of legal words, and 4) a task requiring phonological transformation (Georgiewa et al., 1999). Word and pseudoword reading tasks were performed in an fMRI study, and included 144 dyslexic and non-dyslexic children. The results of this study evidences that dur-

ing phonological analysis, non-dyslexics rather than dyslexics show significantly greater activation in predominantly left hemisphere sites. However, evidence of over activation was revealed in the rightward inferior frontal and medial frontal cortices of dyslexic children, due to an intense remediation reading program on a sentence-level (Meyler et al., 2008). Enhanced (left and right) inferior frontal activation following remediation was also found in several studies on the word-level (Shaywitz et al., 2002). These over activations in the inferior frontal gyrus and have been interpreted as possible areas of compensatory activation. Thus, this might reflect poor reader's additional recruitment of executive resources. Sometimes increased activation was also noted in the homolog of the VWFA, in the right occipitotemporal area, as a response to observed experiences (Shaywitz & Shaywitz, 2008). In general, findings on the location and extent of compensatory mechanisms have not been consistent across investigations. This might occur due to the age of the population examined, or the stage of the recovery process (Eden et al., 2004; Meyler et al., 2008).

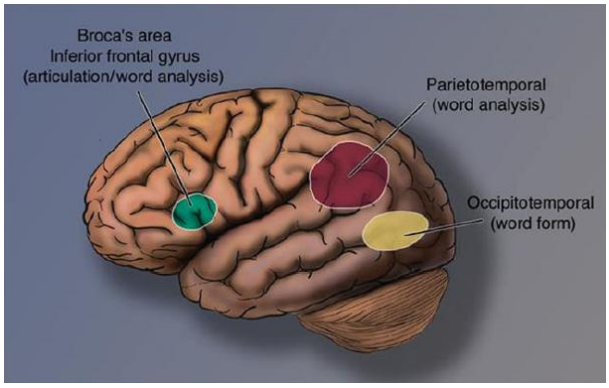

Figure 2 illustrates the neural system for reading. Depicted on the surface of the left hemisphere, there are three important systems relied upon for reading. One is an anterior system in the region of the inferior frontal gyrus (Broca's area), which serves articulation and word analysis. Additionally, there are two posterior systems, one in the parieto-temporal, which serves word analysis, and a second in the occipito-temporal region (the word-form area), which serves the rapid, automatic, fluent identification of words (Shaywitz et al., 2008).

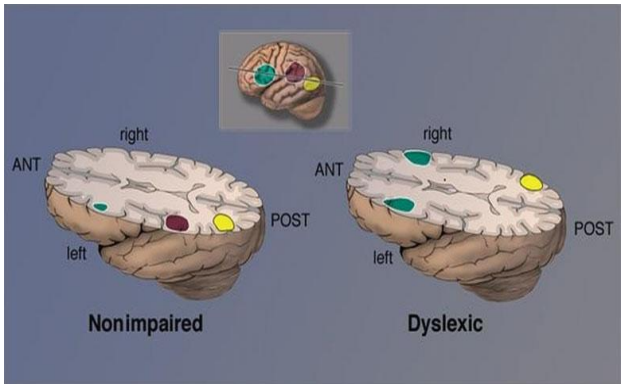

Figure 3 depicts compensatory neural systems and the neural basis for the requirement of extended time for dyslexic students. Non-dyslexic readers activate three leftward neural systems for reading: one anterior and two posterior. Contrarily, dyslexic readers have a disruption in the left hemisphere posterior neuronal systems for reading. In turn they compensate the posterior hypoactivation by developing anterior systems in the left and right hemisphere as well as the posterior rightward homolog of the visual word form area (Shaywitz et al., 2008).

In summary, a number of interrelated neural systems used in reading have been identified in dyslexic readers. There were impairments observed in at least two posterior brain regions, one the pareitotemporal system (supramarginal gyrus; angular gyrus) and one in the occipitotemporal system (VWFA). These posterior systems are related with an anterior system. Also in the dyslexics' ante-

riro systems, distinct regions were observed to be under or over-activated (see Figure 2 and 3 for details) (Shaywitz et al., 2008).

EEG- and MEG Data of the Pre-lexical Component

Functional methods other than fMRI have been used to study dyslexia, namely electroencephalography (EEG) and magnetencephalography (MEG). These techniques revealed that reading elicits a negative waveform between 150 and 250 ms after stimulus onset over occipito-temporal regions. This print sensitive component, namely the N170, seems to reflect pre-lexical analysis, because the response does not differentiate between words, nonwords or consonant strings (Cornelissen, Tarkiainen, Helenius, & Salmelin, 2003; Salmelin et al., 2004). Additionally, the N170 is related to a form of category-specific visual expertise. This finding was demonstrated by comparing responses between letters and other complex visual stimuli such as human faces or objects (Bentin et al., 1999). While the N1700 effect is for visual expertise of faces and objects, bilateral or predominantly rightward lateralized (Rossion et al., 2003; Tanaka & Curran, 2001). Words evoke as significantly larger negativity over the left compared to the right hemisphere in skilled adult readers (Nobre et al., 1994; Rossion et al., 2003). While adult readers show a left lateralization for processing orthographic information, peaking approximately at 170ms, about ten year old native Italian speaking children demonstrated a negative-going bilateral component, about 200 ms after stimulus onset, on posterior sites (Spironelli & Angrilli, 2009). In non-reading kindergarten children the N170 was absent, and emerged in less than two years after the same children had mastered basic reading skills in 2nd grade (Maurer et al., 2006). An increased N170 over occipito-temporal electrodes on both hemispheres was also observed in non-reading kindergarten children after an eight week (totally 3.6h) training of sound-letter associations (Brem et al., 2010). These findings evidence that hemispheric processing dominance in print is, in children, not entirely automated (Brem et al., 2006; McCandliss et al., 2003b; Polk et al., 2002) and further indicates that a developmental process (neuronal reorganization) is a necessary process through which reading experience drives progressive specialization of a pre-existing inferior temporal pathway dedicated to visual object recognition (Brem et al., 2006; McCandliss et al., 2003b; Polk et al., 2002). It has been suggested that the left lateralization of the N170 for written words is a result of experience, specifically of grapheme to phoneme mapping (Maurer et al., 2005). However, in the case of dyslexic adults, this hemispheric processing preference of letter-string-specific responses peaking about 170ms after stimulus onset, is not observed (Helenius

et al., 1999). Notably, in dyslexic 2nd grade children (compared to their non-dyslexic peers) the N170 response to words was significantly decreased (Maurer et al., 2007).

4 The Theoretical Models of Reading

Whereas spoken language is observed in all societies and has been practiced for hundreds of thousands of years, reading is artificial and rather new, only several thousand years old (Lawler, 2001). A baby exposed to a natural environment results in the development of spoken language. In contrast, print is acquired and must be taught. Learning to read requires multiple skills. Word decoding requires the processing of the visual features first, before the analysis can proceed to content. Words are analyzed first at the level of single letters and then as whole words, later meaning (semantic content) and its sound form (phonology) are activated. Theoretical models of reading are based largely on analysis of behavioral reaction times and error types (Salmelin & Kujala, 2006). According to the theoretical framework of the dual route model (Coltheart, Curtis, Atkins, & Haller, 1993), word decoding is supposed to be achieved through two distinct routes that rely on two different processes (see Figure 4). The grapho-phonological pathway, also called the indirect route, requires visual words to be transformed into their auditory equivalent. This happens when a grapheme is mapped to its equivalent phoneme. This grapheme to phoneme correspondence then in turn allows access to meaning. New encountered words or pseudowords are processed by the grapho-phonological route. The lexico-semantic or direct route relies on the direct association between the visual form of words and their meaning. This association is thought to build progressively when subjects repeatedly encounter words. In languages with a deep orthography, that means that the grapheme to phoneme mapping is not consistent: Only regular words can be processed through the grapho-phonological route. Learned word forms are stored in the long-term memory in a visual word form system, also called the orthographical lexicon. Irregular words, which are previously encountered, are best recognized through the orthographic lexicon (Coltheart, Rastle, Perry, Langdon, & Ziegler, 2001). On the contrary, pseudowords are followed by rules and require the indirect route to be read (Jobard, Crivello, & Tzourio-Mazoyer, 2003).

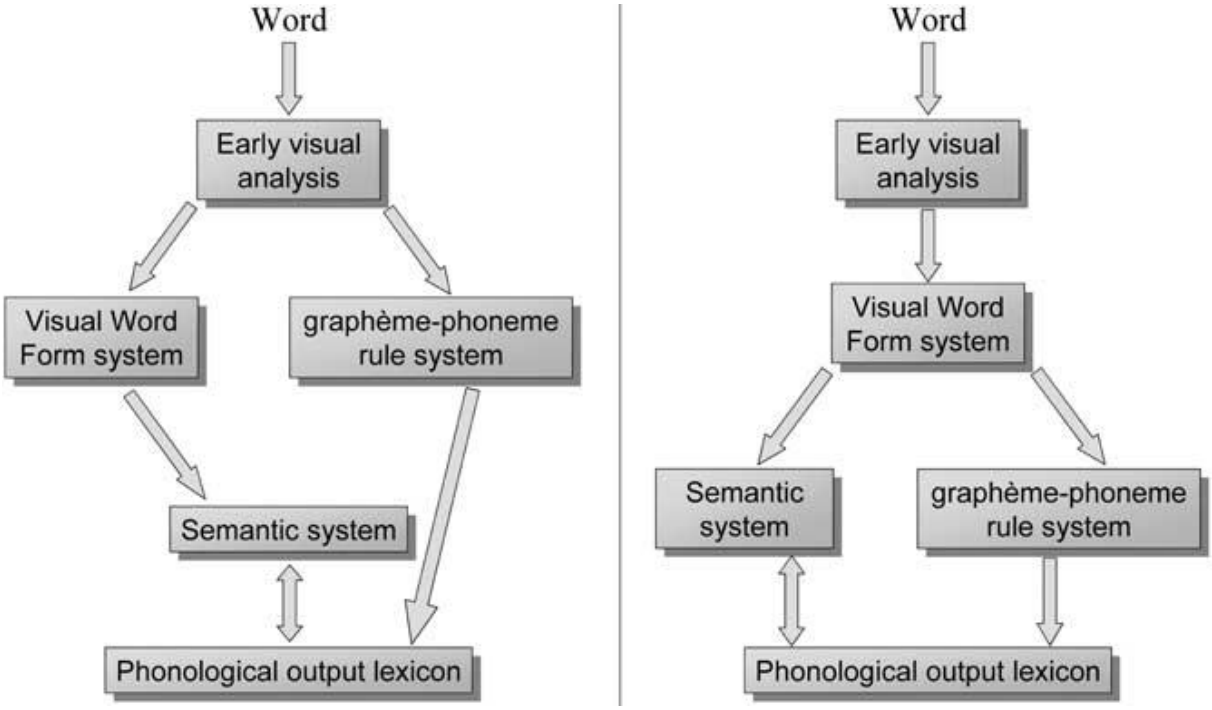

Figure 4 depicts the grapho-phonological, called the indirect route (left) and lexico-semantic, namely direct pathway (right) of reading reflecting the model proposed by dual route theory (Jobard et al., 2003).

In contrast to the dual route model has been a connectionist model proposed (Plaut, McClelland, Seidenberg, & Patterson, 1996). This model assumes that a single indirect route is involved in extracting the statistical regularities between orthography and phonology at different grain sizes. Thus both familiar and unfamiliar words (i.e. pseudowords) are processed by exactly the same network, in which orthography, phonology and semantics are carried out simultaneously in an interactive process. This theory assumes that the amount of exposure to letter strings, rather than their lexical status that influences the behavior of the system (Seidenberg & McClelland, 1989).

5 The Theoretical Frameworks of Spelling

Investigation into the difficulties of processing written language has been focused on the "input" side of the problem – reading. Less attention has been paid on the "output" aspect of written language - writing. Developmental dual-route models of spelling (see Figure 5) (Baxter & Warrington, 1985; Coltheart , Patterson, & Marshall, 1980; Shallice, 1981) have suggested that early acquisition is dominated by either an indirect grapheme-phoneme rule route or direct lexical route (Frith, 1985). The direct lexical route is active when the orthographic property is retrieved by the representation in the othographic lexicon. The indirect (sublexical) route is activated when retrieved information in the case of writing to dictation is abstract and format-independent. This system holds a temporary store, the graphemic output buffer. The output information of the graphemic output buffer is translated into letter shapes. Thus the graphic motor program is developed, leading the execution of corresponding neuromuscular commands (Rapp & Caramazza, 1997).

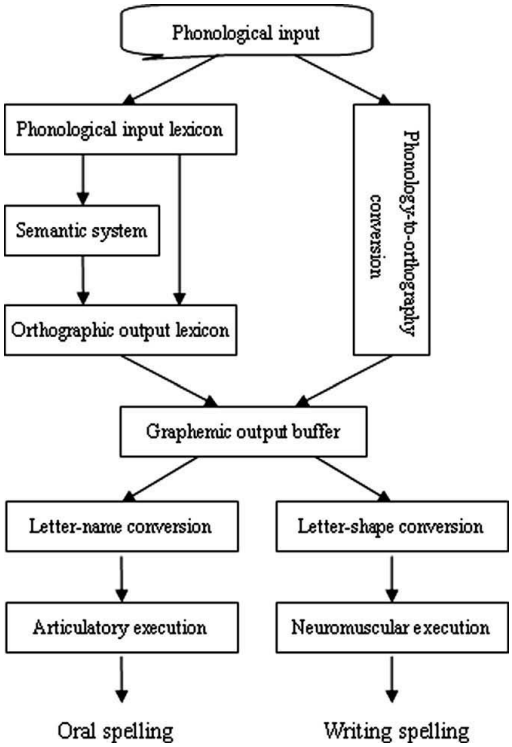

Figure 5 illustrates a model of writing in alphabetic language (Han & Bi, 2009).

In contrast, connectionist theories of developmental spelling models propose that acquisition is characterized by greater elaboration of a single indirect route that maps between phonology and orthography (Sprenger-Charolles, Siegel, Bechennec, & Serniclaes, 2003). Models of

reading have often been assigned to spelling because of the similarities between the two cognitive functions, but spelling is summarized as only the reverse of reading, at least to some extent (Berninger et al., 2006).

It is assumed that developing spelling abilities is a more difficult process than reading skills, based on the observation that the mapping from phonology to orthography is a more irregular and ambiguous process than the reverse (Berninger et al., 2006). The orthographic consistency refers to the degree of systematicity relating phonologic to orthographic mappings. When multiple orthographic renderings are possible for the same sound (e.g. /a:/ in Saal (hall) and Zahl (number)) the consistency decreases (Landerl, Wimmer, & Frith, 1997; Peereman, Dufour, & Burt, 2009).

The theoretical framework determining the cognitive architecture of spelling is an endogenous generation of serial behavior: letters are produced one at a time and must be produced in the correct order (Lashley, 1951). The basic questions are: "How is the order of the elements in a sentence represented?" and "What are the specific characteristics of the mechanisms that ensure that the elements are selected and produced in their proper order?" (Goldberg & Rapp, 2008). A number of mechanisms and representations have been proposed and examined as possible serial-order systems in cognitive domains. One model suggests an output mechanism (consisting of the response representations and an implementation of the competitive output process) and an activating mechanism, which is responsible for establishing an appropriate gradient of activation over the output representations . Orthographic representations are assumed to contain information about abstract letter identities and their order. Form-independent orthographic representations are processed by a working memory system – the graphic buffer. This system maintains the active orthographic information during the serial selection of the letters that is required for their production (Goldberg et al., 2008).

Reading and spelling of words employs a lexical semantic system that is also shared with spoken word processing (Tsapkini & Rapp). The orthographic lexicon, which corresponds to the long-term memory, is the key component of the lexical system (Goldberg et al., 2008). By repeated processing of orthography, 'memory traces' are formed in long-term memory (Plaut et al., 1996). Word-specific memories are commonly referred to as lexical representations. The orthographic representations are consolidated and refined over many reading and writing exposures . It is often (but not exclusively) presumed that these representations are stored as localized units or entries in a "mental lexicon" (Plaut et al., 1996) . Inadequacies in the phonological representations have deleterious effects on performance (Goswami, Ziegler, & Richardson, 2005)

6 Methods

The empirical section within this thesis refers to two established methods used in the field of neuroscience to investigate cognitive processes in the brain, namely electroencephalography (EEG) and functional magnetic resonance imaging (fMRI). The two techniques rely on different correlates of neural activity and additionally provide different advantages and disadvantages. The EEG measures the neuronal electrical activity derived on the surface of the scalp and provides an excellent time resolution in the range of milliseconds, however it is limited by poor spatial resolution. In contrast, fMRI relies on activity induced blood perfusion changes and allows the identification of brain areas involved in cognitive processes with a fairly high spatial (mm) and low temporal resolution. The following section gives a brief introduction to our use of these methods, so as to offer context for the data acquisition and analysis in the empirical section.

6.1 Electroencephalography

Electroencephalography (EEG) is a non-invasive technique used to record the oscillation of brain electric potentials with a high temporal and low spatial resolution. For measuring the EEG signal, electrodes are placed on the surface of the scalp with standardized configurations (Jasper, 1958). Electrical activity arising from large patches of synchronously active neurons is recorded. The active cortical neurons produce currents spreading passively through the brain, cerebrospinal fluids, skull and the scalp. Finally, these currents reach the scalp surface, upon which the voltage differences between each electrode and the reference electrode are computed.

The EEG oscillations are mainly generated by postsynaptic potentials of pyramidal cells in the cortex. A cortical neuron has a typical resting potential of -70 µV. Neural activity is produced by releasing neurotransmitters in the synaptic gap, whereas signals are transmitted from one neuron to the target neuron. The synaptic activity can either produce excitatory (EPSP) or inhibitory (IPSP) postsynaptic potentials across the membrane of the target neuron. Hence, neural activity is accompanied by a negative or positive shift of the resting state. IPSP produces inhibitory effects on the target neuron. EPSPs facilitate the generation of an action potential (depolarization). The EPSP allows the inflow of positive ions from the extracellular to the negative charged intracellular space. The shift in postsynaptic potentials induces an elec-

trical dipole. Electrical dipoles are derived on the cortical surface when several thousand cortical neurons are active synchronously and neurons are aliened orthogonal to the cortical surface. Notably, EEG signals are the measures of larger, summed activity, of thousands of synchronously active cortical neurons arranged in parallel.

Event Related Potentials

Event related potentials (ERPs) are small changes in the electrical activity of neuronal populations which appear time-locked to the occurrence of a sensory, motor or psychological event. This external event produces positive and negative going waves of peaks in the EEG signal. ERP peaks are classically identified on the basis of polarity (positivity, negativity), latency and scalp distribution, or by a combination of these values (see Figure 6). ERPs are computed by the averaging the time-locked brain responses of several events. The averaging of the events and in particular the sum of the brain responses measured at a certain electrode is effectual. This procedure enables the reduction of random occurring noise, also present in the measured signal. With an increasing number of stimuli presented to the subject, the signal to noise ratio can be improved.

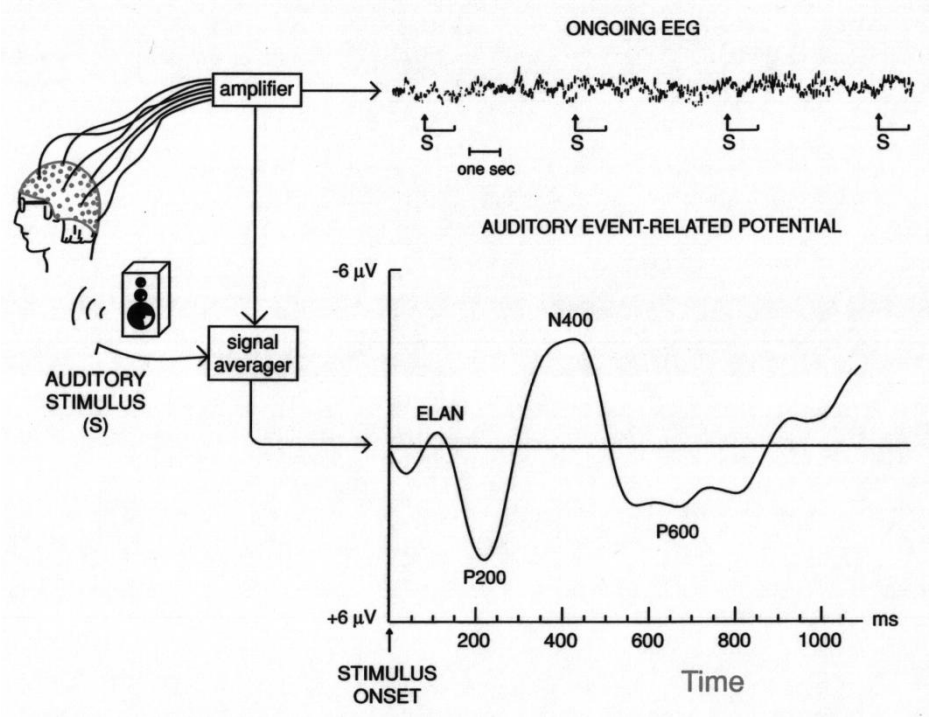

Figure 6 illustrates the EEG technique**.**

6.2 Functional Magnetic Resonance Imaging

The magnetic resonance imaging (fMRI) technique provides images of the brain regions that are active during the performance of a specific task. Thereby the fMRI allows the mapping of specific cortical activity indirectly by measuring the blood-oxigen-level-dependent (BOLD) singal change (hemodynamic response). fMRI offers very high spatial resolution (in the range of millimeters) and low temporal resolution (in the range of seconds). The time course of the hemodynamic response (see Figure 7) takes advantage of the differential magnetic properties of oxygenated and deoxygenated hemoglobin. While deoxy-hemoglobin is paramagnetic, oxy-hemoglobin is diamagnetic. The processing of specific information in the brain activates neurons and causes the transportation of more oxygenated blood to that location. After an initial decrease of oxy-hemoglobin due to consumption of oxygen (initial dip) the blood flow increases which leads to a change of the local ratio between oxy-hemoglobin and deoxy-hemoglobin (hemodynamic response). The oxygen supply overcompensates the neuronal need (Fox & Raichle, 1986), which results in an increase in the ratio between oxy- and deoxygenated blood. Due to the afformentioned different magnetic properties between oxy- and deoxygenated hemoglobin, the "Blood-Oxygen-Level-Dependent" (BOLD) contrast arises (Ogawa, Lee, Nayak, & Glynn, 1990). This corresponds to an increase in the MR-signal. The signal intensity rises in a maximum of 5 to 8 seconds from stimulus onset and returns after 10 to 16 seconds back to baseline. After the diminishing of the oversupply of oxygenated blood, it still takes some time for the blood volume to return to baseline.

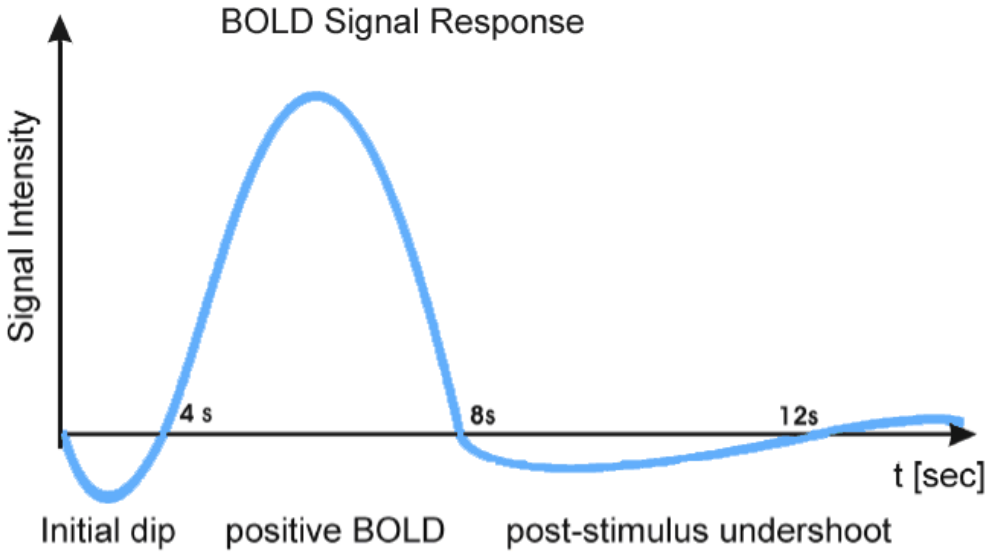

Figure 7 depicts the time-course of the BOLD signal (hemodynamic response)

7 Aims and Relevance of the Thesis

The principal purpose of the present work is to contribute to a better understanding of dyslexic's impaired reading and spelling processes. This work especially focuses on investigating the phoneme to grapheme mapping that is, according to the phonological deficit theory, impaired in dyslexic individuals. Since an efficient and reliable association between phonemes and graphemes is fundamental for successful reading and spelling, the investigation of this process allows further insight into the neurobiological nature of reading and spelling. This in turn is essential for developing efficient remediation programs. Specific remediation programs are in great need because it is known that when reading difficulties are left unremediated, the academic (Shaywitz, 2003), social, emotional and economic consequences of reading problems can be profound and far-reaching (Meyler et al., 2008). However, fruitful remedial efforts need longstanding and specific treatment. The present work aims to investigate the functional correlates of DD by using EEG and fMRI. Additionally, this work aims to evaluate the efficiency of a multi-sensory computer based spelling program. The learning software, namely Dybuster, is being developed at the department of computer science at the ETH of Zurich under the leadership of Prof. Markus Gross. The goal of this collaboration was to improve the effectiveness of the multi-modal computer program while simultaneously gaining further insight into the mechanism underlying spelling behaviors.
In the first study, using EEG, we focus our investigation into the reading process of dyslexic and non-dyslexic 8 to 12 year old children. In keeping with the theoretical framework that assumes visually presented print elicits reliable electrical potentials over occipitotemporal electrodes in an early time course (peaking about 150 to 250 ms after stimulus onset), the present study focuses on the examination of this prelexical component. This prelexical component reflects the conjunction of letters into the integrated visual percept (i.e. phoneme to grapheme mapping) and is developed through experience.

A second study was designed to examine phoneme to grapheme mapping, which is essential for word decoding, in dyslexic and non-dyslexic adults. Since word decoding is a multisensory task, whereas the visually presented orthographic representation has to be mapped to the corresponding sounds (phonological representation) we aimed to investigate the audiovisual integration of words by using EEG. The EEG method offers an excellent temporal resolution of amplitudes in the range of milliseconds and permits investigation of the time course for word decoding, specifically.

The third study is a follow up study of the second study. In this study the investigation was focused on the audiovisual processing of words and pseudowords, by using fMRI. We assume that in contrast to words, which are processed in accordance with the dual route theory via the lexico-semantic pathway, pseudowords are processed by the grapho-phonological pathway. Therefore, decoding pseudowords might involve, more explicitly, the phoneme to grapheme mapping. In contrast to the EEG, the fMRI technique is characterized by a high spatial resolution. This permits identification of proper and deficient networks between the dyslexic and non-dyslexic adults in very specific terms.

The purpose of the forth study is to examine the newly implemented phonological cue and the enhanced word selection controller designed to refelct a phoneme-based student model. In accordance with the phonological deficit theory, dyslexic individuals are characterized by poor phoneme to grapheme mapping, and by extension poor verbal associative learning. In this study we aimed to investigate if the additional phonological information provided by the spelling program improves spelling acquisition. Additionally, our aim was to gain deeper insight into which factors are relevant for acquiring spelling skills. To accomplish this, we analyzed the influence of cognitive abilities, such as attention functions and behavioral memory skills, on the learning behavior of the dyslexic and non-dyslexic children.

8 Empirical Part

8.1 Experiment I: ERP Differences of Prelexical Processing between Dyslexic and Non-dyslexic Children

Monika Kast[1], Stefan Elmer[1], Lutz Jäncke[1] & Martin Meyer[1]

[1]Department of Neuropsychology, University of Zurich, Switzerland

Published in International Journal of Psychophysiology, Volume 77, Issue 1, Pages 59-69

Abstract

The present Event Related Potential (ERP) study aimed to investigate group differences in the early processing stages of 36 dyslexic and 24 non-dyslexic 8-12 year old children, while performing a lexical decision (word/pseudoword judgment) task.

Our data showed larger amplitudes of negative-going waveforms in non-dyslexic children than dyslexic children over occipital/occipitotemporal electrodes, at about 220 ms after stimulus onset. This electrophysiological response has previously been identified in adult readers and labeled as the N170 component. Notably, as reflected by the topographic maps, children, irrespective of group, processed the linguistic stimuli bilaterally and we did not observe any differences in ERP parameters between words and pseudowords, within groups. Behavioral responses indicate that words were recognized more quickly than pseudowords, irrespective of group.

By applying post-hoc ROI-analyses based on a source estimation approach (sLORETA) we observed that non-dyslexic participants, when compared to dyslexic children, demonstrated significantly stronger current density over the left-hemispheric inferior temporal lobe when processing pseudowords.

We concluded that impaired reading is reflected by the decreased amplitude of the early lexical component N170. The lack of a left hemispheric processing preference in both groups and similar activation for words and pseudowords can be considered as a lack of reading experience and a less established reading system in children. Our results indicate that dyslexic children commit fewer specialized neuronal circuits for processing print and confirm the reasoning that acquiring reading skills requires cortical reorganization over occipito-temporal regions.

Introduction

Dual Route Theory of Reading

One of the defining characteristics of dyslexic individuals is an inability to recognize and decode words accurately and efficiently (Adams, 1990; Lyon, 1995). Therefore, understanding the neurophysiological underpinning of illiteracy has received significant interest. According to the theoretical framework of the dual route theory word, reading can be achieved through two distinct routes that rely on two different processes. The graphophonological route, also called the indirect route, requires visual words to be transformed into their auditory equivalent. This happens when a grapheme is mapped to its equivalent phoneme. This grapheme to phoneme correspondence then in turn allows access to meaning. The lexicosemantic or direct route relies on the direct association between the visual form of words and their meaning. This association is thought to build progressively when subjects repeatedly encounter words. Therefore, learned word forms are stored in the long-term memory in a visual word form system, also called the orthographical lexicon (e.g.(Coltheart et al., 1993). The model of the dual route theory assumes that words may have been encountered by readers already and are therefore present in the visual word-form lexicon. In contrast, pseudowords require the indirect route to be read (Jobard et al., 2003).

The Electrophysiological Correlate of Reading

The initial stages of reading correspond to the specialized visual brain processes that occur within 200 ms of stimulus presentation in occipito-temporal regions (McCandliss, Cohen, & Dehaene, 2003a). Reading related activation spreads along the ventral surface of the temporal lobe from posterior to anterior regions (e.g. Pammer et al., 2004). Visually presented words, pseudowords, strings of consonants, strings of alphanumeric symbols and strings of forms evoke a sharp negative peak in adults at about 170 ms after stimulus onset (Bentin et al., 1999; Rossion et al., 2003). Children show a longer latency in the N170 (Spironelli et al., 2009). The N170 recorded from intracranial electrodes is interpreted as being sensitive to abstract, orthographic word form properties (Nobre et al., 1994) and is described as reliably distinguishing between word-like stimuli and visually matched symbol strings (Bentin et al., 1999; Tarkiainen, Helenius, Hansen, Cornelissen, & Salmelin, 1999). Precisely because the N170 represents the earliest recognition component of linguistic material in adults, it has been characterized as the ‘pre-lexical word processing component’(Spironelli et al., 2009). In addition, the N170 is related to a form of category-specific visual expertise. This is shown by find-

ings that reveal a negative deflecting wave peaking around 200 ms for all visual stimuli when the ERP responses to letters are compared with other complex visual stimuli such as human faces or objects (Bentin et al., 1999; Bentin et al., 2007). While the N170 effect is bilateral or predominantly right lateralized for visual expertise of faces and objects (Bentin, Allison, Puce, Perez, & McCarthy, 1996; Rossion et al., 2003; Tanaka et al., 2001), word processing is found to evoke significantly larger negativities over the left hemisphere in adults (Nobre et al., 1994; Rossion et al., 2003). Notably, it has been suggested that the N170 for faces and the N170 for words are driven by distinct forms of perceptual processing, because there were habituation effects revealed for faces, yet none for words (Maurer, Rossion, & McCandliss, 2008a). The aforementioned left hemispheric dominance for word processing is increased in skilled readers (McCandliss et al., 2003a; Salmelin, Helenius, & Service, 2000). While adult groups show left sided lateralization effects for orthographic and phonological as well as orthographic tasks peaking approximately at 170 ms, a study with ten year old native Italian speaking children demonstrated a negative going bilateral component, posterior activation 200 ms after stimulus onset, as a response to visually presented Italian words (Spironelli et al., 2009). The lack of hemispheric processing dominance evidences that reading in children is not yet entirely automated, as automatic skilled reading is associated with hemispheric processing preference (Brem et al., 2006; McCandliss et al., 2003a; Polk et al., 2002).
It has been suggested that a developmental process is necessary through which reading experience drives progressive specialization of a pre-existing inferior temporal pathway dedicated to visual object recognition (McCandliss et al., 2003a), and that left lateralization of the N170 for written words is a result of experience, specifically of grapheme to phoneme mapping (Maurer et al., 2005). As emerging readers learn to decode letters and words, a form of perceptual expertise emerges. Letters become rapidly and effortlessly conjoined into the integrated visual percepts. This is a pivotal process in developing fluent reading ability (Maurer et al., 2007). Neuroimaging studies indicate that visual word form perception corresponds to a functional specialization in the middle part of the left fusiform gyrus, located in the occipito-temporal region. This area in the ventral inferotemporal cortex has been associated with the visual word form area, or VWFA (Cohen et al., 2000; Cohen et al., 2002; Dehaene et al., 2002).

Developmental Dyslexia

Developmental dyslexia is characterized by low reading and writing skills in spite of an average IQ, good educational support and solid social background (World health organization,

2009). The core problem of dyslexia seems to be a phonological processing problem (Bradley et al., 1983; Ramus et al., 2003c). However, this theory is not able to explain the general auditory (Baldeweg et al., 1999; Farmer et al., 1995; Reed, 1989; Tallal, 1980), visual (Livingstone et al., 1988; Lovegrove et al., 1980; Stein et al., 1997) and motor impairments (Nicolson et al., 1990; Rudel, 1985; Wolff et al., 1990) dyslexic individuals often suffer from. The phonological processing deficit hypothesis claims poor phonological awareness. Poor phonological awareness manifests as impairment in the phoneme to grapheme conversion (Frith, 1985). In literate adults, this phoneme to grapheme mapping occurs rapidly and automatically (Paulesu et al., 1996) and can be considered an over-learned paired association process (van Atteveldt et al., 2007). However, in the case of developmental dyslexia, a high level of letter to speech-sounds association may never be reached (Vellutino et al, 2004).
The reading problems in developmental dyslexia have been investigated in previous neurophysiological studies. A magnetencephalography (MEG) study revealed that the letter-string-specific responses peaking around 150 ms were prevalently processed over left hemispheric occipito-temporal regions in fluent readers. This hemispheric processing preference was not observed in dyslexic adults (Helenius et al., 1999). In non-reading kindergarten children the N170 was absent and emerged in less than two years of reading training (Maurer et al., 2006). Notably, the N170 in response to words was significantly decreased in dyslexic 2nd grade children compared to their non-dyslexic peers (Maurer et al., 2007).

Aim of the Present Study

While several neurophysiological studies have investigated the processing of word-like stimuli in adults, it is not well known to date what the neurophysiological underpinnings of word form, lexical, and meaning-related information are, specifically at the early stages of word recognition in dyslexic versus non-dyslexic 8 to 12 year old children. Working with the theoretical framework that early phases of cortical processing and visually presented stimuli elicit reliable electrical potentials over occipito-temporal regions, the present study focuses on examining electrophysiological responses to visually presented words and pseudowords in dyslexic and non-dyslexic children. In line with this, in the present study we investigated the 'pre-lexical component' peaking at around 200 ms after stimulus onset. The pre-lexical component reflects the conjunction of letters into the integrated visual percept (phoneme to grapheme conversion).
Additionally, our study aims to test predictions based on the dual route theory with respect to processing differences of words and pseudowords in children. According to the dual route

theory, pseudowords are processed via the graphophonological (indirect) route while words are represented in a mental lexicon. Greater negative going activation elicited by pseudowords (vs. words) in occipital electrodes during early processing stages has been reported in several previous studies (Hinojosa, Martín-Loeches, Muñoz, Casado, & Pozo, 2004; Martin-Loeches, Hinojosa, Gomez-Jarabo, & Rubia, 1999; Rudell, 1991). This effect has sometimes been referred to as the "recognition potential" and was interpreted as a function of an enhanced lexical search for pseudowords. (Contrary to this research, it is important to note that some studies show conflicting interpretations, i.e. a lack of different activation patterns for pseudoword or word stimuli (Maurer, Zevin, & McCandliss, 2008b; Wydell, Vuorinen, Helenius, & Salmelin, 2003). In a previous study eleven year old dyslexic (vs. non-dyslexic) boys showed decreased N100 amplitudes in response to pseudowords over rightward centro-parietal regions. The authors explained that processing of pseudowords requires high attention and therefore the decreased amplitude regions reflect an attention deficit in dyslexic children. Poor readers, according to the authors, may prefer to reduce their attention to a limited number of letters during the processing of complex and long pseudowords. Thus, the strategic reduction of attention may result in their difficulties with phoneme to grapheme mapping (Wimmer, Hutzler, & Wiener, 2002). Thus, we expected to find that dyslexic children demonstrate a different activation pattern (at least in one of the following parameters: amplitude, latency or hemispheric processing dominance) in reading words and pseudowords, when compared to non-dyslexic children. This difference should reflect the different expertise dependent proficiencies in the specialized visual processing of letters and word-like stimuli, such as the less automatic process in phoneme to grapheme mapping in dyslexic individuals. Moreover, we assume that words are presented better in the mental lexicon in non-dyslexic children and are retrieved more quickly when compared to pseudowords. We presume that dyslexic individuals, who are characterized by problems of phoneme to grapheme mapping, process words and pseudowords similarly.

In addition to standard ERP analyses, this study aimed at identifying group differences in current density by applying a low resolution topographic approach for source estimation, sLORETA. In accordance with the literature, which indicates a progressive specialization process of visual word recognition reflected by morphological alterations in the ventral inferotemporal cortex (McCandliss et al., 2003a), we expected different activation patterns over the left inferior temporal lobe and more precisely over the fusiform gyrus during the early processing stages at around 200 ms after word/pseudoword onset.

Materials and Methods

Subjects

Thirty six dyslexic children (10.27 ± 0.93 SD years of age, 11 females and 25 males, 30 right and 6 left handed) and 24 non-dyslexic children (9.92 ± 0.94 SD years of age, 11 females and 13 males, 22 right and 2 left handed) with ages ranging from 8 to 12 years participated in this study. Their handedness was assessed by the Annett (1970) questionnaire. All children had normal or corrected to normal vision, were native Swiss-German speakers with an IQ > 85. Children with an IQ below 85 were excluded from the study.

Dyslexic children were recruited via therapists or school psychological services. The dyslexic children were categorized as dyslexic if their scores in the standardized writing- and reading-tests were below the 10th percentile. Non-dyslexic children showed standard reading and writing skills. All of the children's parents gave their informed consent for this study, as required by the Declaration of Helsinki. Experimental procedures were approved by the Ethics Committee of the University of Zurich.

Procedure and Stimuli

Every child who participated in an EEG experiment underwent a series of standard psychological tests in a separate session previous to the EEG recording. The test battery included classical German orthography ("Salzburger-Lese und Rechtschreibtest SLRT" (Landerl et al., 1997) or "Diagnostischer Rechtschreibtest für fünfte Klassen DRT5" (Grund, Haug, Naumann, & Weinheim, 1995)) and reading tests („Zürcher Lesetest ZLT" (Linder & Grissemann, 2000)) as well as pseudoword reading ("Salzburger-Lese und Rechtschreibtest SLRT" (Landerl et al., 1997a)) in order to quantify writing and reading errors. A standard German intelligence test (HAWIK III (Tewes & Rossmann, 1999)) was also administered to ensure that the children possessed average or above average general cognitive skills (IQ > 85). In two cases the IQ-data was provided by the school psychologist. HAWIK-IV and K-ABC were each applied once. The testing took place no longer than three months before our data acquisition. We decided not to administer an additional IQ test. Notably, both tests showed that the general IQ is not subdivided into performance intelligence and verbal intelligence.

Procedure

During the EEG experiment participants were seated in a dimmed and acoustically shielded room, approximately 100 cm from a screen. The subjects' chins were propped on a scaffold in

order to minimize artifacts during EEG recording. The subjects were instructed to fixate on a small cross at the center of the screen and keep as still as possible, and to especially avoid blinking. Ninety disyllabic nouns were visually presented for 4000 ms. The words consisted of five letters each, with a difficulty range from 8 to 11 (mean difficulty 9.39 and mean frequency of 1758, according to the European Corpus Initiative Multilingual Corpus I ((ECI/MCI), Korpus Ger03). Additionally, 90 disyllabic pseudowords (consisting of the same letters as the nouns) were shown, also for 4000 ms. An example for a word was "Sonne" (sun) which has the difficulty 10 and the frequency 1228. The pseudoword corresponding to "Sonne" was "Nonse". The difficulty level was determined by factors such as doubling of letters as in "Kasse" (cashpoint), silent letters such as "Lehre" (lesson) or phoneme – grapheme difficulties illustrated in words like "Kurve" (bend). Volunteers were asked to decide whether the presented letter string was a word or a pseudoword by pressing a mouse button as fast as possible with the index finger of the right hand. During the stimulus interval, which lasted 2000 ms, a small fixation cross appeared. The stimuli were randomly presented by the presentation software (www.neurobs.com) during the course of three runs, each lasting about 4 minutes.

EEG Recording and Analysis

The EEG data was continuously recorded from 29 channels and with 2 zygomatic eye channels operating with a sampling rate of 500 Hz and a band pass filter (0-100 Hz) using an EEG-amplifier (Brainproducts, Munich, Germany). The silver/silver-chloride electrodes (Ag/AgCl) were located using the international 10-10 system: Fp1, Fp2, F7, F3, Fz, F4, F8, FT7, FC3, FC4, FT8, T7, C3, Cz, C4, T8, TP7, CP3, CPz, CP4, TP8, P7, P3, Pz, P4, P8, O1, Oz, O2. The reference electrode was placed at FCz and two EOG electrodes were located below the outer canthus of each eye. The impedance was reduced below 5kΩ. The software used for the off-line analysis was Brain Vision Analyzer (Version 1.04, Brainproducts, Munich, Germany). The data was high- and low-pass filtered off-line at 0.1-30Hz and re-referenced to an average reverence. Eye-movements were removed using an independent component analysis (ICA) (Jung et al., 2000). Artifacts exceeding ±100μV were automatically rejected and other artifacts were manually eliminated. The synchronized processed data was segmented in 1100 ms epochs, baseline corrected relative to the -100 to 0 ms pre-stimulus time and averaged for each participant and stimulus type. In addition, grand means were averaged for each group (dyslexics, controls) as well as across all subjects. Moreover, electrodes over occiptiotemporal (P7, P8) and occipital (O1, O2) regions were clustered on the left and

right hemisphere. The ERP analysis was calculated over these posterior pooled electrode pairs (see Figure 8).

The time windows for computing all statistical analysis were defined according to two consecutive global field power (GFP) minima of the grand average of each condition across all subjects. The GFP is a time varying measure of map amplitude computed as the spatial root mean square (RMS) (derived from all EEG channels). Peaks were automatically detected for each participant within the time windows defined by GFP N170 for correctly judged words (172-276 ms) and correctly judged pseudowords (172-276 ms).

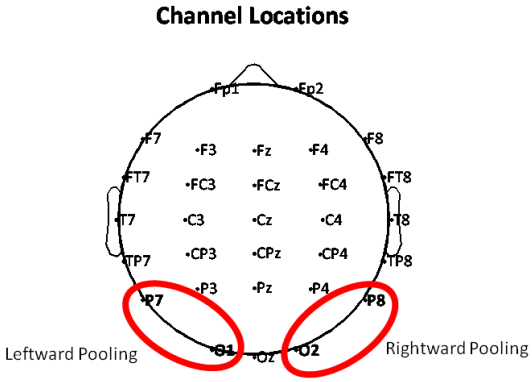

Figure 8: Channel locations. The posterior occipito-temporal and occipital electrodes were clustered on the left and right hemisphere together. Thus, ERPs analysis was applied over these electrode pairs.

After removing bad trials and incorrectly judged stimuli, there were, from the 90 presented words and 90 pseudowords, the following number of trials included in the statistical analysis: The data of controls consisted of 67.6 (75.2%) correctly judged words and 66.1 (73.5%) correctly judged pseudowords. In dyslexic individuals, 61.2 (68%) correctly judged words and 58.2 (64.7%) correctly judged pseudowords were included.

Source Estimation

Standardized low resolution electromagnetic tomography (sLORETA; (Pascual-Marqui, 2002) http://www.uzh.ch/keyinst/NewLORETA/sLORETA/sLORETA.htm) was used to estimate the electrical source of the N170, defined by the time window of the global field power (GFP). sLORETA is an electrical brain imaging technique and employs a current density estimate given by the minimum norm solution. The localization inference is based on standardized values of the current density estimates (Pascual-Marqui, 2002). It has been shown that low resolution electromagnetic tomography is efficient when compared to linear inverse algorithms and has been successfully used in recent EEG studies on auditory cognition (Meyer, Baumann, & Jancke, 2006; Meyer, Elmer, Baumann, & Jancke, 2007; Zaehle, Jancke, Herr-

mann, & Meyer, 2009) sLORETA computes 3D linear estimations (sLORETA solutions) for the EEG inverse problem, standardized with respect to instrumental and biological noise, as mathematically defined in the original paper by (Pascual-Marqui, 2002). Estimations are computed within a three-shell spherical head model including scalp, skull and brain compartments. The brain compartment is restricted to a cortical gray matter model co-registered to the Talairach probability brain atlas, digitized at the Brain Imaging Center of the Montreal Neurological Institute (Talairach & Tournoux, 1988). The solution space was restricted to the cortical grey matter and provided 6239 voxel at 5 mm resolution.

In order to define adjusted time windows for the N170 we calculated the peaks over the leftward and rightward pooled occipital and occipitotemporal electrodes. Thus ± 5 ms from these peaks, which lasted from 220 – 236 ms, were taken as relevant time windows for illustration of the current density distribution. This time window was applied for all conditions as well as for both hemispheres and for both groups.

Furthermore, a post hoc region-of-interest (ROI) analysis was calculated in sLORETA to investigate significant current density differences between groups (dyslexic/ non-dyslexic), conditions (word, pseudoword) and hemisphere (left, right). The selected ROIs were discussed in literature to play a pivotal role during written language processing at about 200 ms after stimulus onset and thus defined in the inferior temporal gyrus. The landmarks of ROIs are determined by an automatic anatomical labeling procedure implemented in sLORETA that is based on the position, size and borders of Brodmann areas in stereotactic 3D Talairach space (Talairach et al., 1988). Differences in source density were only calculated for the time window from 220 – 234 ms. The volume that corresponds to our ROI includes BA20 and BA37 (see Figure 9). While BA20 consisted of 109 voxels, on the left as well on the right side, with a resolution of 5 mm, BA 37 included 96 voxels of the left and 88 voxels on the right hemisphere. Note that in the present study we preferred to refrain from using the notions of Brodmann Areas and used anatomically more appropriate terms namely inferior temporal lobe and fusiform gyrus instead.

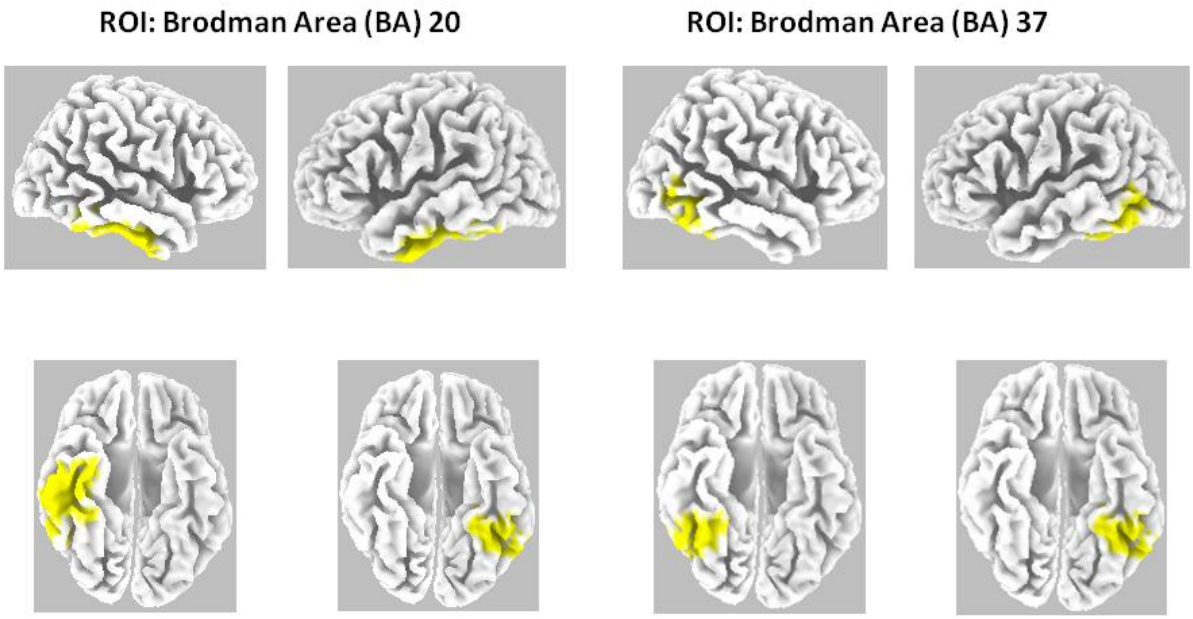

Figure 9: ROIs were determined in the inferior temporal lobe (BA 20) and fusiform gyrus (BA 37). Current densities were estimated by standardized low resolution electromagnetic tomography software, namely sLORETA.

Statistical Analyses

Individual peaks were automatically identified in the GFP-based latency band for each test subject. Differences in N170 amplitude and latency between hemispheres (left/ right), conditions (correctly judged word/ correctly judged pseudoword) and group (dyslexics/ non-dyslexics) were tested computing a 2x2x2 independent analysis of variance for repeated measurements (ANOVA) over the pooled electrodes. The left sited posterior occipito-temporal/ occipital cluster consisted of the electrodes P7 and O1, while the right hemispheric cluster included the electrodes P8 and O2. To disentangle significant effects of the main ANOVA the computation was split into smaller variance analyses. To test the hemisphere effect two stripped 2x2 ANOVAs with the independent variables hemisphere (left/ right) and group (dyslexic/ non-dyslexic) were calculated for words and pseudowords separately. For evaluating condition effects two 2x2 variance analyses with the factor condition (word/ pseudoword) as within-subject and group (dyslexics/ non-dyslexics) as between-subject factor were calculated for both hemispheres (right/ left) separately. Additionally, post-hoc t-tests were applied to explain the significant interactions.

Because ROI-data were not normally distributed as revealed by the Kolmogorov-Smirnov-test, a logarithmical transformation (lg10) was applied (e.g. Fridlund, 1991; Gaddum, 1945). By applying this procedure we ensured the normal distribution of data, which allowed parametric statistical calculations. Thus separate ANOVAs for repeated measures for the inferior

temporal lobe and fusiform gyrus with the within-subject factors, hemisphere (left/ right) and condition (word/ pseudoword), as well as the between-subject factor group (dyslexic/ non-dyslexic) were computed based on the data defined from the sLORETA ROI analysis. Additionally, the global ANOVA was split into a smaller variance analysis with the independent variables hemisphere and group. This ANOVA was calculated for pseudowords and words separately. Moreover, two individual ANOVAs were applied for the left and right hemisphere ROIs with the independent variables condition (pseudoword/ word) and group (dyslexic/ non-dyslexic). Post hoc t-tests were applied to explain significant interactions.

Results

Behavioral Data

Nonparametric testing (Mann-Whitney U test) was applied where the descriptive data we collected or the results of the standardized psychological tests were either ordinal scaled or not normally distributed according to the Kolmogorov-Smirnov-test. The outcome of the descriptive data revealed that the two groups (dyslexic/ non-dyslexic) did not significantly differ in their age ($t_{(58)}$=-1.431, p=0.158) or school grade (Mann-Whitney Z =-0.837, p=0.403). The analysis of the IQ performances revealed no group differences in the performance intelligence ($t_{(56)}$=-1.202, p=0.234), whereas the groups differed significantly in the verbal intelligence ($t_{(56)}$=-2.891, p=0.005) and general intelligence ($t_{(58)}$=-2.345, p=0.022). Regardless of these results both groups showed an at least standard IQ (see Figure 10). Additionally, the statistical procedure revealed highly significant different reading and writing performances between the two groups (see for details Table 1).

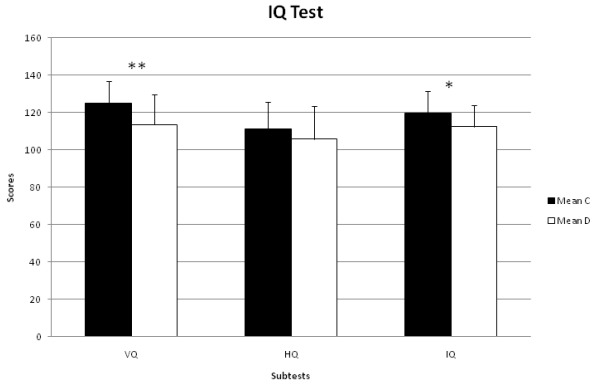

Figure 10: Results of the IQ data. There was no group differences in the performance intelligence revealed, while non-dyslexic children performed significantly better in the verbal and general IQ. However, all children had an IQ > 85. * depicts significance, $p < 0.05$, ** illustrates significance, $p < 0.01$.

Table 1: Behavioral data for the investigated samples. This table depicts the data of standardized reading (ZLT and SLRT) and writing (SLRT or DRT5) tests of the dyslexic and non-dyslexic children.

	Dyslexic (n=36)				**Non-dyslexics (n=24)**				**Mann-Whitney Z**	
Measures	**Mean**	**S.D**	**Min.**	**Max**	**Mean**	**S.D**	**Min.**	**Max**	**score**	**Probability**
ZLT: word list reading time (z)	-1.94	1.00	-3.00	-0.30	-0.11	0.89	-0.8	1.2	-5.40	<0.001
ZLT: word list reading error (z)	-1.91	0.98	-3.00	1.20	0.06	0.92	-1.30	1.75	-5.67	<0.001
ZLT: text reading time (z)	-1.60	1.32	-3.00	1.00	0.23	1.43	-3.00	2.05	-4.19	<0.001
ZLT: text reading error (z)	-2.00	1.02	-3.00	0.30	0.54	1.32	-1.40	3.00	-5.69	<0.001
SLRT: reading words similar pseudowords time (z)	-0.99	0.80	-2.35	1.10	0.11	0.70	-0.80	1.30	-4.52	<0.001
SLRT: reading words disimilar pseudowords time (z)	-0.84	0.88	-2.60	1.10	0.11	0.90	-1.70	1.30	-3.76	<0.001
spelling performance (z)	-1.44	0.56	-2.60	0.40	-0.17	0.71	-1.00	1.30	-5.84	<0.001

	Frequency	**Frequency**
Gender (m/f)	25 / 11	13 / 11
Handedness (r/l/a)	30 / 6 /0	22 / 2 /0

The behavioral data collected during the EEG-experiment were analyzed for accuracy and reaction time. The data of accuracy were not normally distributed and therefore the Mann-Whithney U-Test was applied. Dyslexic children identified significantly fewer words (Z= -3.454, p= 0.001) and pseudowords (Z =-3.014, p=0.003) correctly. Thus, dyslexic children had significantly more errors in identifying words (Z=-3.454, p=0.001) and pseudowords (Z=-3.014, p=0.003). The data of reaction times were analyzed by applying a 4x2 ANOVA with the independent variables answer type (pseudoword correctly judged/ pseudoword erroneously judged/ word correctly judged and word erroneously judged) and group (dyslexic/ non-dyslexic). The outcome of these procedures revealed a significant effect for answer type ($F_{(1,58)}$= 7.785; p= 0.007) and a significant interaction between answer type x group ($F_{(1,58)}$= 4.95; p= 0.03), but no main group effect. The post-hoc t-test revealed a significant group effect for responding to pseudowords incorrectly ($t_{(58)}$-2.570, p= 0.0128) (two tailed). We applied two post hoc t-tests for dependent samples for dyslexic and non-dyslexic children individually to disentangle the answer type x group interaction and proofing processing differences of words and pseudowords within groups. This calculation yielded a significant effect for processing words and pseudowords correctly ($t_{(23)}$= 0.273, p< 0.001) for the non-dyslexic group. Dyslexic children showed different reaction times for correctly judged words compared to pseudowords ($t_{(35)}$=6.593, p<0.001) as well as for erroneously judged words compared to erroneously judged pseudowords ($t_{(35)}$=2.264, p=0.03) (see Figure 11).

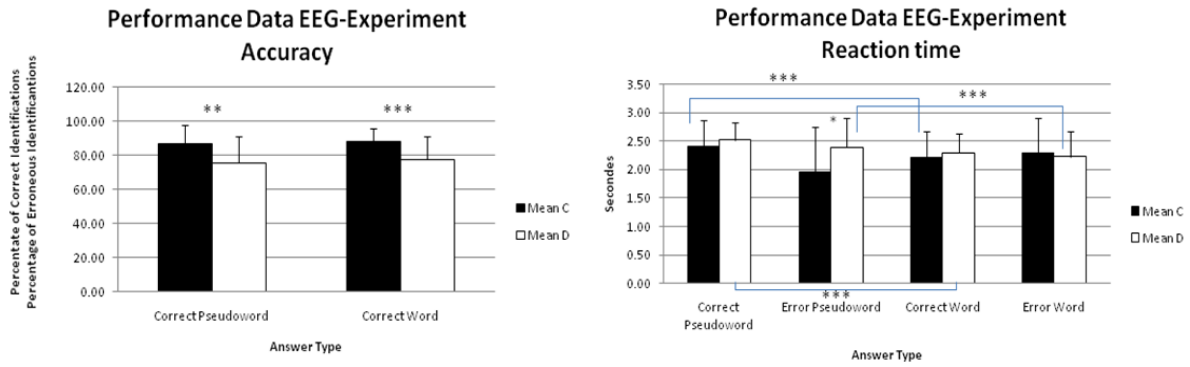

Figure 11: Behavioral answers (accuracy and reaction time) of the word/pseudoword judgment task (correct identification and erroneous responses). Control children (C) identified significantly more words and pseudowords correctly and made significantly less errors compared to dyslexic children (D). There were no group differences in the reaction time of correctly processed stimuli. However, both groups processed words more quickly than pseudowords. * depicts significance, $p < 0.05$, ** illustrates significance, $p < 0.01$ and *** shows significance, $p < 0.001$.

N170 Responses to Words and Pseudowords over Left- and Right Sited Posterior Areas

Group Differences for Word and Pseudoword Reading

Figure 12 shows ERP curves for the two conditions (only correctly judged stimuli) separately for both groups collected from the pooled occipito-temporal with occipital electrodes (left: P7&O1/ right:P8&O2). In particular, an unambiguous N170 component was observed in the two conditions (words/ pseudowords) and hemispheres (left/ right) at about 220 ms after stimulus onset in both groups (dyslexic/ non-dyslexic). This figure also depicts the amplitudes of the N170 component. Figure 13 shows the topographic maps for correctly judged words and pseudowords in both groups.

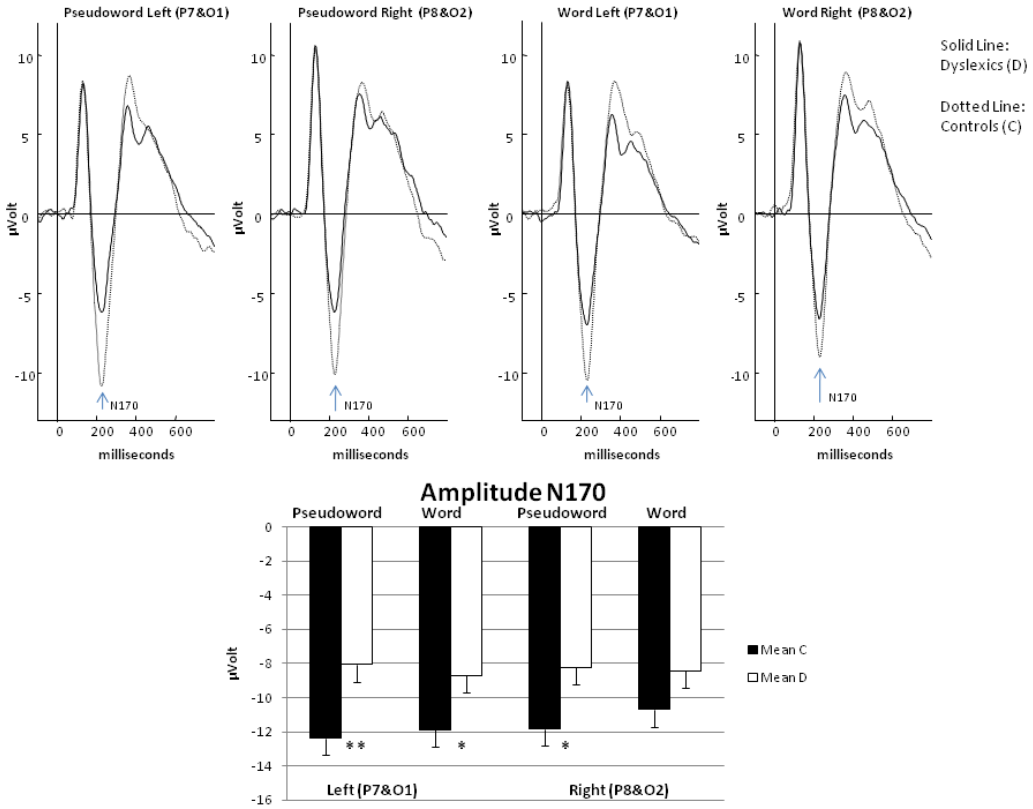

Figure 12: Leftward and rightward ERPs over posterior electrodes during word – pseudoword processing. The upper Figure illustrates the ERPs while the lower plot illustrates the peak activity. Dyslexic children (D) showed compared to non-dyslexic children (C) decreased amplitudes for word and pseudoword reading over the left and for pseudoword reading over the right hemisphere. * depicts significance, $p < 0.05$, ** illustrates significance, $p < 0.01$.

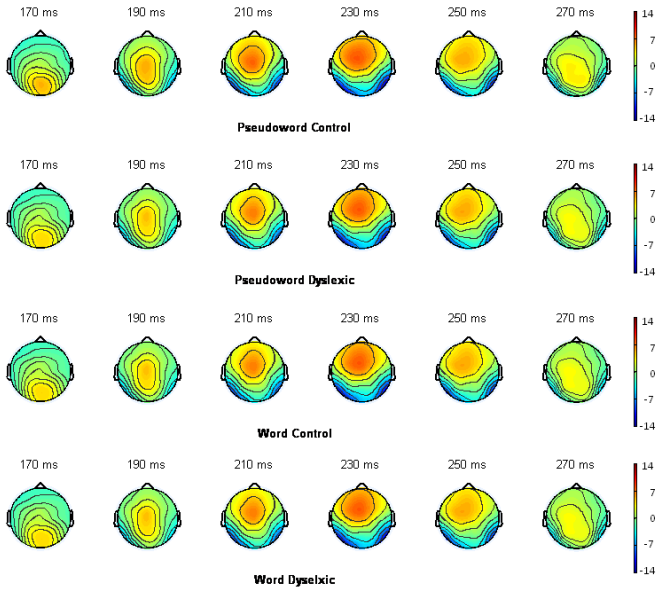

Figure 13: Topographic maps over all electrodes for processing words and pseudowords in dyslexic and non-dyslexic children. The topographic maps illustrate the dipoles of the time courses for word and pseudoword reading in dyslexic and non-dyslexic children. It shows that the posterior negativity occurs in the two groups and for both conditions after 200 ms of stimulus onset.

Amplitude Analysis

We computed a global 2x2x2 ANOVA for repeated measurements with the within-subject factors: hemisphere (left/ right) and conditions (words/ pseudowords) and the between-subject factor: group (dyslexic/ non-dyslexic) for the N170 latency band. The outcome of this analysis revealed a significant condition x group interaction ($F_{(1,58)}$=4.014, p=0.0498) and a significant group effect ($F_{(1,58)}$=6.854, p=0.0113).

To disentangle the condition x group interaction we calculated two smaller 2x2 ANOVAs with the independent variables condition (word/ pseudoword) and group (dyslexics/ non-dyslexics) over both hemispheres (left/ right) separately. The outcome of these procedure revealed a main effect group ($F_{(1,58)}$= 6.781, p=0.0117) over the left hemisphere. Over the right hemisphere we observed a significant group effect ($F_{(1,58)}$= 4.534, p=0.0375) and by lowering the threshold we noted a condition x group interaction ($F_{(1,58)}$= 3.484, p=0.067).

To further elucidate the main effect of group we computed four post-hoc t-tests (one-tailed) for independent samples. The results of these post-hoc comparisons showed significantly enhanced amplitudes for non-dyslexic compared to dyslexic individuals when reading pseudowords over the left ($t_{(58)}$=-2.974, p=0.0021) and right hemisphere ($t_{(58)}$=-2.435, p=0.0090) and when reading words over the left hemisphere ($t_{(58)}$=-2.119, p=0.0192). By lowering the threshold dyslexics show decreased amplitudes compared to non-dyslexic children for word reading over the right hemisphere ($t_{(58)}$=-1.660, p=0.0512).

Latency analysis

The global 2x2x2 ANOVA for repeated measurement with hemispheres (left/ right) and conditions (pseudoword/ word) with the within-subject factors and group (dyslexic/ non-dyslexic) as between-subject factor revealed no significant effects. By lowering the threshold there was a significant group effect revealed ($F_{(1,58)}$=3.539, p=0.065).

Source estimation (LORETA) while Processing Words and Pseudowords

To explore the electrophysiological sources of the N170 component we performed two post-hoc ROI analyses for both word and pseudoword processing. For this purpose we computed two separate 2x2x2 ANOVAs with the independent variables condition (pseudoword/ word), hemisphere (left/ right) and group (dyslexic/ non-dyslexic) over the fusiform gyrus (BA 37) and the inferior temporal lobe (BA 20) (see Figure 9). The outcome of this statistical procedure revealed a significant hemisphere effect ($F_{(1,58)}$=34.08, p<0.001) for the inferior temporal lobe. To disentangle the hemisphere effect, we calculated two smaller 2x2 ANOVAS with the independent variables hemisphere (left/ right) and group (dyslexic/ non-dyslexic) for pseudo-

words and words independently. The variance analysis for pseudowords revealed a main effect hemisphere ($F_{(1,58)}$=26.78, p<0.001) and by lowering the threshold a group effect ($F_{(1,58)}$=3.65, p=0.061). The 2x2 ANOVA for words yielded a main effect for hemisphere ($F_{(1,58)}$=25.40, p<0.001). Additionally, we applied a 2x2 variance analysis with the within-factor condition (words/ pseudowords) and between-factor group (dyslexic/ non-dyslexic) for the left and right hemisphere independently. We found a main group effect ($F_{(1,58)}$=4.133, p=0.0467) for the left hemisphere. The post-hoc t-test revealed a significant group difference for processing pseudowords on the left hemisphere ($t_{(58)}$=2.326, p=0.0236) (see Figure 14). The analysis of the fusiform gyrus ROI did not provide any significant effects.

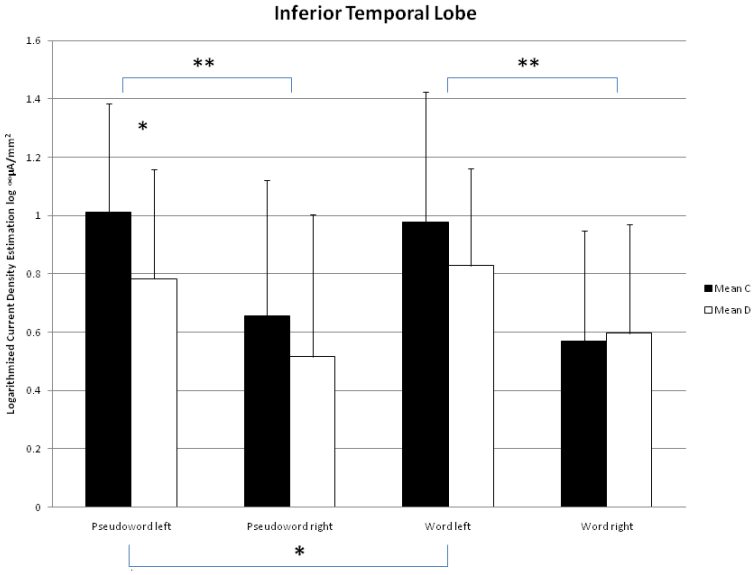

Figure 14: ROI analysis of the inferior temporal lobe for word and pseudoword reading. The global ANOVA revealed a highly significant hemisphere effect. The current density is in both groups for pseudowords as well as words on the left (vs. right) hemisphere enhanced. Additionally, there was a significant group difference on the left hemisphere for pseudoword reading found. * depicts significance, $p < 0.05$, ** illustrates significance, $p < 0.01$.

Discussion

The present ERP-study was designed to investigate the time-course and the neurophysiological correlates of processing words and pseudowords in dyslexic as well as non-dyslexic children. Notably, the dyslexic children we investigated were characterized by both poor reading and poor spelling skills. We first introduce the behavioral data. The discussion section is arranged in four main parts. First, we discuss the most interesting finding, namely the electrophysiological differences between dyslexic and non-dyslexic children during the early stages of reading, for both words and pseudowords, apparent in the N170 latency band. Second, we discuss the missing lateralization effect of processing linguistic material in dyslexic as well as

non-dyslexic children. Third, we interpret the word and pseudoword processing in both groups. Fourth, we discuss the results revealed by applying a source estimation approach (sLORETA).

Behavioral Data

The behavioral data showed group differences for accuracy. Non-dyslexic children correctly identified words and pseudowords significantly more often than their dyslexic peers. This finding underscores the notion that non-dyslexic children read more accurately. With regard to reaction times, we did not observe group differences for correctly processed words and pseudowords. However, the reaction time of incorrect responses for pseudowords was significantly lower in dyslexic individuals. The interpretation of erroneously processed stimuli is difficult because the result is ambiguous. It is not clear whether children were not able to detect the stimuli correctly or pressed the wrong button by accident. Therefore we refrained from either analyzing or interpreting incorrectly responded trials. The most interesting finding provided by our behavioral data was the highly significant result that both non-dyslexic and dyslexic individuals process words faster than pseudowords. This finding indicates that words might be represented in a mental lexicon and are processed, as suggested by the dual route theory (e.g. Coltheart et al., 1993)), through the direct route, whereas pseudowords have to go through an indirect pathway.

Decreased N170 Amplitude in Dyslexic Children

It is of particular note that our data revealed significantly smaller amplitudes in the N170 component over posterior regions for dyslexic compared to non-dyslexic children. This finding was yielded in the left hemisphere for both word and pseudoword reading and only for pseudoword reading in the right hemisphere. Additionally, a condition by group interaction was found. No latency differences were found between the two groups. The N170 for adults, which occurs about 200 ms after stimulus onset in children, reflects experience-dependent neural changes in several forms of visual expertise (e.g. faces or objects) including expertise for visual word form properties. This expertise is generated in the occipitotemporal brain areas (Nobre et al., 1994) and it has been suggested that these brain areas could accommodate ensembles of neurons specialized in the recognition of letters, graphemes or words, and that they are likely to be intermixed with other neurons involved in object and face recognition (Puce, Allison, & McCarthy, 1999). Our findings show that dyslexic children show less activation in a component that is sensitive to visually presented stimuli and which modulates as a

function of accumulated experience. We reason that the previously mentioned component reflects impaired reading and implicates deficient processing in areas especially suited for visual recognition. These findings are in line with the results of Maurer and colleagues (2007) who studied a group of children with risk of dyslexia and a group with no risk of dyslexia while in kindergarten and 2nd grade. While they found that kindergarten children who developed dyslexia showed an atypical development in the speed with which visual brain processes became specialized for print. On the other hand, during the course of time from kindergarten to 2nd grade, dyslexic children did not increase the amplitude in the print specialized component (Maurer et al., 2007). While the N170 in non-reading kindergarten children was absent, this component has been shown to emerge in less than two years, after the same children had mastered basic reading skills in 2nd grade. When comparing the magnitude of the N170 of 2nd graders with that of adults, adults were found to exhibit a magnitude-decrease of the N170 (Maurer et al., 2006).

Our observation also agrees with an assumption proposed by McCandliss and coworkers (2003). McCandliss et al. claim that occipitotemporal brain areas are partially plastic and can, during ontogenesis, become progressively attuned to the requirements of reading. Thus, dyslexic children might be characterized by slower plastic reorganization in occipitotemporal brain areas. We can therefore draw the conclusion that plastic reorganization in occipitotemporal regions is an important process for acquiring fluent reading skills. Since reading skills are dependent on both ontogenetic factors and experience we would have preferred to build subject groups with small age-ranges. In both groups investigated, the average subject age was about 10 years and the subjects were in the middle of their third grade. The age range of four years might also bear a large variance in our ERP-data. Previous fMRI data revealed that both dyslexic and non-dyslexic children of about 11 years of age activate the same main areas during reading (van der Mark et al., 2009). This path breaking finding from van der Mark and colleagues (2009) indicates that the impaired reading is mandatorily linked to a dysfunctional VWF-system.

Missing Lateralization Effect for Word and Pseudoword Reading in Children

While studies that investigated adult readers found a left lateralized N170 for visually presented words, pseudowords and strings of consonants (e.g. Maurer et al., 2008b; Nobre et al., 1994; Rossion et al., 2003), our data collected from children did not reveal this left hemispheric processing dominance. The absence of the clear leftward processing preference for visually presented letter strings in both dyslexic and non-dyslexic children underpins the

notions that explain asymmetric language processing in adults: It can be interpreted as the proper state of maturation or as a result of acquiring specific reading expertise. Accordingly, it takes children several years to develop an expertise in word recognition (Aghababian & Nazir, 2000). However, Grossi and colleagues (2001) published a developmental ERP-study investigating subjects ranging from 7 to 23 years. These authors already observed a shift from the right to the left hemisphere in 9 year old children by processing visually presented rhyme and non-rhyme words (Grossi, Coch, Coffey-Corina, Holcomb, & Neville, 2001). It has to be noted that the Swiss school system starts with reading at about the age of 7, therefore the 9 year old children participating in our study might have less reading experience than the volunteers in the Grossi and colleagues (2001) study, which investigated individuals living in America.

According to previous imaging studies the emergence of expertise correlates with the amount of activation in the 'VWFA' by letter strings in non-dyslexic and dyslexic children (McCandliss et al., 2003a; Shaywitz et al., 2002; Temple, 2002). Thus there is no ready-made 'module' for visual word recognition but rather a progressive specialization process that capitalizes on the plasticity of the human ventral inferotemporal cortex to build the 'VWFA' (Cohen & Dehaene, 2004). In addition to positing acquired reading expertise through training, the plastic reorganization theory (McCandliss et al., 2003a) claims a developmental process during maturation. There might be a pre-existing inferior temporal pathway for visual object recognition that is progressively wrought through experience.

Similar Processing of Words and Pseudowords in Children

Our third main result demonstrated a lack of electrophysiological differences between word and pseudoword processing in the N170 for both the dyslexic and non-dyslexic individuals. We merely found a significant condition x group interaction. Whereas non-dyslexic individuals show a rather enhanced amplitude for pseudowords compared to words, in dyslexic children the amplitude is increased during word (vs. pseudoword) reading. We suggest that non-dyslexic children recognize words as words and can therefore decode them with less effort than pseudowords. According to the dual route theory words are stored in the mental lexicon whereas pseudowords have to be processed by the grapho-phonological pathway. Dyslexic children do not show this processing advantage for words and probably process them probably more similarly to pseudowords. However, ERP-responses to words and pseudowords imply comparable underlying processes irrespective of groups.

,Studies comparing word and pseudoword processing so far have displayed inconsistent findings. Some studies have found that, in adults, greater negative going activation was evoked for pseudowords than for words over occipital electrodes, peaking at about 170 ms after stimulus onset; however, other studies did not replicate this finding (Maurer et al., 2008b; Wydell et al., 2003). Maurer and collegues suggested that N170 amplitude responses might be dependent on the task and presentation mode. It is unclear whether the different findings of word and pseudoword processing effectively depend on task and presentation modes or on the subject's different reading strategies. It is known that younger children often process pseudowords more similarly to real words than older children and adults (Coch & Holcomb, 2003). It has been claimed that the concept of 'word-likeness' develops throughout the early elementary-school years (Henderson & Chard, 1980, p.101). The reaction time differences intra groups for correctly judged words and words indicate that both groups process words compared to pseudowords more quickly. This finding underscores the notion that already children represent written words in the mental lexicon. Nevertheless, our results also agree, to some extent, with the dual-route model proposed by (Coltheart et al., 1993). It is known that adults establish the word superiority effect (Reicher, 1969) as a result of several years of reading experience. We found the word superiority effect only in our behavioral, not in our electrophysiological data.

The N170 we observed is most prominent over occipito-temporal/occipital regions and is meant to reflect aspects of elementary visual processing. Our study did not show differences in N170 parameters between word and pseudoword processing. This observation is interpretable as demonstrating both words and pseudowords undergoing the same visual processing before the phonological stages of language decoding occur. On the other hand we noticed differences in the N170 amplitude between dyslexic and non-dyslexic children, which indicate that the non-dyslexic individuals are not able to appropriately decode the visual features of presented words at a prelexical stage. Thus, this data pattern can be taken as evidence for the existence of a distinct graphophonological route which appears to function deficiently in dyslexic children. In line with this finding, Maurer and collegues (2005) suggest that sound-to-letter mapping recruits occipito-temporal regions. With respect to the lexicosemantic route, our data do not provide either corroborating or challenging evidence as we did not observe any significant effects in the N400 latency band.

Less Activation in the Inferior Temporal Cortex in Dyslexic Children

Generally, we found the most prominent group activation differences over posterior scalp areas. This posterior activation could also be shown by means of a source estimation device (sLORETA). A stronger current density was revealed over the leftward (vs. rightward) inferior temporal cortex in the two groups for words and pseudowords. Additionally, we found enhanced current density in non-dyslexics, when compared to dyslexics, on the left hemisphere, while processing pseudowords. This finding is in accordance with results of neuroimaging studies as outlined in turn. It is strongly suggested that there is a lexical pathway spreading along the ventral temporal lobe from the posterior to the anterior regions. In the left occipitotemporal/fusiform regions with extension into the middle and inferior temporal gyri, a fast visual word processing system was localized by Sandak and coworkers (2004). Other authors proposed a more specific region and localized the 'VWFA' in the left mid-fusiform gyrus (Cohen et al., 2002; McCandliss et al., 2003a) and thus claimed that this area is progressively recruited for fast visual word recognition in the course of reading development.

Conclusion

The data of our study bore four interesting findings. We primarily evidenced a decreased N170 in dyslexic compared to non-dyslexic children during a lexical decision task. The N170 is a component sensitive to the recognition of visually presented stimuli and discriminates between complex visual stimuli and words. Thus, dyslexia might be characterized by the impaired recognition of letters during an early stage of reading, which is characterized by visual feature recognition rather than lexicosemantic access.

The second finding our child-derived data yielded was the missing left hemispheric lateralization effect for language-based stimuli. This result underpins the notion that automation and expertise, and thus leftward asymmetry, are a result of reading experience and are hence not yet necessarily present in the average ten year old child. Therefore, reading experience leads to the shaping and establishing of left hemispheric neural networks in the temporal region. This process should be considered a form of "plastic reorganization" that is not fully finalized in children.

The third result of our ERP data was the similar processing of words and pseudowords in children irrespective of group. We suggest that this effect is the result of a lack of extensive reading experience in children. However both groups identified words more quickly com-

pared to pseudowords. Our data support the notion that words and pseudowords must, to some extent, be represented in the mental lexicon differentially.
The fourth finding of the present study resulted from assumption free source estimation and suggests that the neural circuit in the inferior ventral cortex may account for the left hemisphere processing preference.
In essence, the present study provides novel evidence as it shows that specific modulation of event-related brain responses flag impaired reading proficiency in dyslexic when compared with non-dyslexic children, irrespective of the semantic content of language.

Acknowledgment

This project was supported by the fund 56234102 of the Forschungskommission & Nachwuchsförderung of the University of Zurich and SNF-grant 320000 – 120661/1.
We would like to thank the anonymous reviewers for their detailed and constructive comments that helped to improve this paper.

8.2 Experiment II: Impaired Audiovisual Integration of Linguistic Contents in Dyslexic Adults

Monika Kast*[1], Stefan Elmer*[1], Franziska Blättler[1], Lutz Jäncke[1] & Martin Meyer[1]

[1]Department of Neuropsychology, University of Zurich, Switzerland
*The first and second authors contribute equally to this work

Abstract

The present event-related potential (ERP) study was designed to investigate the neural mechanism sub-serving audiovisual (AV) integration of linguistic contents in 16 dyslexic and 20 non-dyslexic adults. Audiovisual integration was investigated according to the super- or sub-additivity effects, which have been proposed as the principal mechanisms for integration. We recorded EEG-data while disyllabic German nouns were presented either unimodally (auditory or visually alone) or bimodally (AV congruent or incongruent). The global field power (GFP) analyses related to the ERPs revealed enhanced electrophysiological responses for both the audiovisual congruent and incongruent conditions for dyslexic adults compared to non-dyslexic adults in a time range from about 400 to 600 ms. These enhanced electrophysiological responses in dyslexic adults were associated with different topographic maps between dyslexics and non-dyslexics individuals. Furthermore, the dyslexic adults showed stronger GFP magnitudes than the non-dyslexic individuals in the time window (TW) overlapping with the N170 component during processing visually presented nouns. These novel findings indicate a profound association between developmental dyslexia as revealed in adults and audiovisual integration mechanisms. In particular, the differential voltage values we revealed between the two groups at a late time point have been previously shown to support semantic processing. This supports the view that dyslexic adults are characterized by a disturbance in the AV integration of semantic information. The fact that we only found group differences at about 200 ms (i.e. N170 component) during the visual presentation lends support to the argument that the auditory information during the audiovisual condition helps compensate the deficit occurring in the visual condition.

Introduction

Phonological Processing Deficit Associated with Developmental Dyslexia

Word decoding can be considered as a bimodal process since it implies that the visually processed orthography becomes amalgamated with the auditory processed phonology (Ehri & Wilce, 1980; Ziegler & Goswami et al., 2005). Accordingly, phonological codes are processed automatically and sub-serve visual word recognition (Frost, 1998; Rastle & Brysbaert, 2006). In skilled readers the efficient association of orthographical and phonological codes can be considered as an over-learned process (van Atteveldt, Formisano, Blomert, & Goebel, 2007a) that occurs rapidly and automatically (Paulesu et al., 1996). However, in the case of developmental dyslexia (DD) the establishment of an efficient letter to speech-sound association, which is essential for word decoding may never take place (Vellutino et al., 2004).

DD is generally characterized by poor word decoding and spelling skills in spite of an average IQ, conventional education, and solid social background (World health organization, 2009). According to the phonological deficit theory, affected individuals show a specific impairment in the representation, storage and/or retrieval of speech sounds (Bradley et al., 1983; Ramus et al., 2003b). Additionally, their development of an appreciation for the segmental nature of speech (phonological awareness) has previously been shown to be reduced (Frith, 1985). This is manifested in the impaired phoneme to grapheme mapping skills. Letters and speech sounds are the basic elements of correspondence between written and spoken language. The establishment of culturally defined associations of the visual (grapheme) and auditory (phonemes) representations are pertinent for acquiring the decoding skills necessary for reading written words (Byrne, 1998). This grapheme to phoneme association relies on the audiovisual (AV) processing mechanism; it is similar to speech integration (Raij, Uutela, & Hari, 2000; van Atteveldt, Formisano, Goebel, & Blomert, 2004). In line with this assumption, we presume that the AV mechanism essential for word decoding might be impaired in dyslexic individuals.

The Principal Mechanism for Audiovisual Integration

To date, the underlying mechanisms of AV integration are not fully understood (Molholm et al., 2002). Currently, it is suggested that multisensory interactions depend on both (Foxe, 2008) early feedforward (Driver & Noesselt, 2008) and marginally delayed feedback mechanism (Bauer, 2008; Calvert et al., 1999; Driver et al., 2008; Driver & Spence, 2000). Mean-

while, it has been established that neurons in the primary sensory areas typically respond to stimuli in one sensory modality whereas neurons in the association areas, namely, the superior temporal sulcus (STS), the inferior parietal lobe (IPL) (Thompson, Johnson, & Hoopes, 1963), and the insula (Bamiou, Musiek, & Luxon, 2003) respond specifically to the combinations of different modalities, such as, audiovisual stimuli (Benevento, Fallon, Davis, & Rezak, 1977). Previous studies have investigated bimodal integration in the form of super- and sub-additivity effects (Molholm et al., 2002; Molholm et al., 2006; Moran, Molholm, Reilly, & Foxe, 2008). Within this framework the bimodal integration has been proven on the rationale of a greater or a lower response from the bimodal combination of the auditory (A) and visual (V) stimuli, instead of on the sum of the distinctly presented stimuli in one modality (Stanford & Stein, 2007). Thus, the neural basis of bimodal integration was assessed by subtracting the ERPs of the summed A and V stimuli (presented alone) from the ERP of the AV combination of the stimuli [i.e., AV > (A + V) or AV < (A + V)] (Calvert & Thesen, 2004). Previous ERP-studies compellingly demonstrated that the neural responses to simultaneously presented AV stimuli diverge from the summed ERPs of the stimuli presented in either the V or the A domain. This finding evidences that simultaneously and distinctly presented AV stimuli are not processed in the same way (Giard & Peronnet, 1999; Molholm et al., 2002). To date, most of the research pertaining to AV integration has been conducted on either animals (Benevento et al., 1977; Bodner, Kroger, & Fuster, 1996; Schroeder & Foxe, 2002; Seltzer & Pandya, 1980), or humans; it has incorporated studies using simple non-linguistic stimuli (Foxe & Schroeder, 2005; Murray et al., 2004; Schroeder et al., 2002). Nevertheless, little is currently known about AV integration in written language processing.

Theoretical Framework for Word Decoding

According to the theoretical framework of the dual route theory (Coltheart et al., 1993; Coltheart et al., 2001), word decoding is supposed to be achieved through two distinct routes that rely on two different processes. The grapho-phonological pathway, also called the indirect route, requires visual words to be transformed into their auditory equivalent. This occurs when a grapheme is mapped to its equivalent phoneme. This grapheme to phoneme correspondence is the prerequisite required, in order to access a words meaning. Consequently, newly encountered words or pseudowords are processed by the grapho-phonological route. The lexico-semantic or direct route relies on the direct association between the visual form of words and their meaning. This association is thought to grow progressively if subjects repeatedly encounter words. As a result, learned word forms are stored in the long-term memory; in

particular in the visual word form system, namely, the orthographical lexicon (Coltheart et al., 2001; Jobard et al., 2003).

The initial stages of reading correspond to specialized visual brain processes that occur within 200 ms of stimulus presentation over occipito-temporal regions (McCandliss et al., 2003b). Visually presented stimuli in general, such as, words, pseudowords, strings of consonants, strings of alphanumeric symbols, and strings of forms evoke a sharp negative peak at around 170 ms after stimulus onset in adults (Bentin et al., 1999; Rossion et al., 2003). Reading related activation spreads along the ventral surface of the temporal lobe from the posterior to the anterior regions (Pammer et al., 2004).

Aim of the Present Study

The present ERP-study was specifically designed to examine the electrophysiological correlates of AV integration of disyllabic nouns in 16 dyslexic and 20 non-dyslexic adults. Since an efficient association of phonemes to graphemes is essential for word decoding, the present work aimed to contribute to a better understanding of AV processing of linguistic contents in dyslexic adults. Notably, learning to associate a given grapheme with a certain phoneme evidently corresponds to both enhanced and depressed synaptic responses (Bear, 1996). Based on this reasoning, we are not able to predict whether word decoding, which requires to some extent grapheme to phoneme mapping, elicits diminished or enhanced neuronal responses in dyslexic adults. This is due to the fact that, only a few studies have investigated AV integration mechanism in dyslexic individuals to date.

Previous fMRI studies have investigated the neuronal underpinnings of unimodal (V, A) and bimodal (AV congruent or AV incongruent) letter-speech sound associations. The findings from these studies have revealed lower activation of the bilateral superior temporal cortex during the integration of letters and speech sounds in dyslexic vs. non-dyslexic adults (Blau, van Atteveldt, Ekkebus, Goebel, & Blomert, 2009). Furthermore, dyslexic compared to non-dyslexic children exhibited bilaterally reduced neural responses in the planum temporale, Heschl's sulcus, and superior temporal sulcus during a task requiring AV integration of letters (Blau et al., 2010). Meanwhile, a magnetencephalography (MEG) study investigating non-impaired adult readers reported magnetic field deflections in the N1/P2 time window (TW) reflecting processes that occur during the integration of graphemes and phonemes (Raij et al., 2000).

In the context of the present study, we hypothesize that dyslexic adults exude a different neuronal activation pattern during the AV integration of words [AV> (A+V), as AV< (A+V)]

compared to non-dyslexic adults. This assumption is based on the phonological processing deficit theory (Bradley et al., 1983; Ramus et al., 2003c), which posits that dyslexic individuals possess impairments in the representation, storage and/or retrieval of phonological information, as well as a reduced phoneme to grapheme conversion. Due to previous findings revealing AV integration effects during letter to sound associations (Raij et al., 2000; van Atteveldt et al., 2004), we assume that AV integration may occur in a similar way during single words processing. Therefore, we expect to discover differential integration processes between the two groups as a result of the impaired AV mechanisms seen in dyslexic individuals.

Methods

Participants

Sixteen dyslexic (28.06 ± 6.24 SD years of age, 8 female and 8 male, 14 right-handed and 2 left-handed) and 20 non-dyslexic adults (28 ± 4.7 SD years of age, 8 female and 12 male, 20 right-handed) participated in the present study. Their handedness was assessed by a questionnaire (Annett, 1970). Dyslexic volunteers were diagnosed during their childhood by professional therapists. To test the current spelling performance of dyslexic individuals, they completed a standardized spelling test based on the German language "Rechtschreibungstest" (Kersting & Althoff, 2004). Of our 16 dyslexic research participants, 9 performed below the 10^{th} percentile on this standardized spelling test based on the German language and seven attained scores above the 10^{th} percentile. The average score that dyslexic adults perceived on the spelling test was 19.2 percent. In order to ensure that low reading and spelling performance were not associated with general low intelligence, we included an IQ test in our battery (HAWIE-R (Tewes, 2001)). IQ scores were above 85 (with a mean in: general IQ: 119.5; verbal IQ: 115.8, and performance IQ: 117.5) in all dyslexic subjects. Seven of the dyslexic participants had a university education and nine had completed an apprenticeship. Our non-dyslexic subjects were students from the University of Zurich who had no prior history of poor spelling or reading skills. All participants were native Swiss-German speakers, had no history of neurological or psychiatric disorders, and gave written consent in accordance with the Declaration of Helsinki. The local ethics committee has approved this study.

Procedure and Stimuli

During each EEG session research participants were seated in a dimmed, acoustically shielded room, at a 100 cm distance from the computer screen. The subjects propped their head on a scaffold, in order to avoid movement related artifacts. Additionally, they were instructed to fixate their eyes on a small cross at the center of the screen, to keep as still as possible, and especially to try and avoid blinking their eyes. During the experiment eighty disyllabic, abstract or concrete German nouns were presented either auditorily (A) (i.e., "Scheibe" *pane*) or visually (V) (i.e., "Wolke" *cloud*), audiovisually congruent (AVc) (i.e., auditorily = "Betrug" *fraud*, visually = "Betrug" *fraud*), or audiovisually incongruent (AVi) (i.e., auditorily = "Fenster" *window*, visually = "Pflanze" *plant*) (see Figure 15).

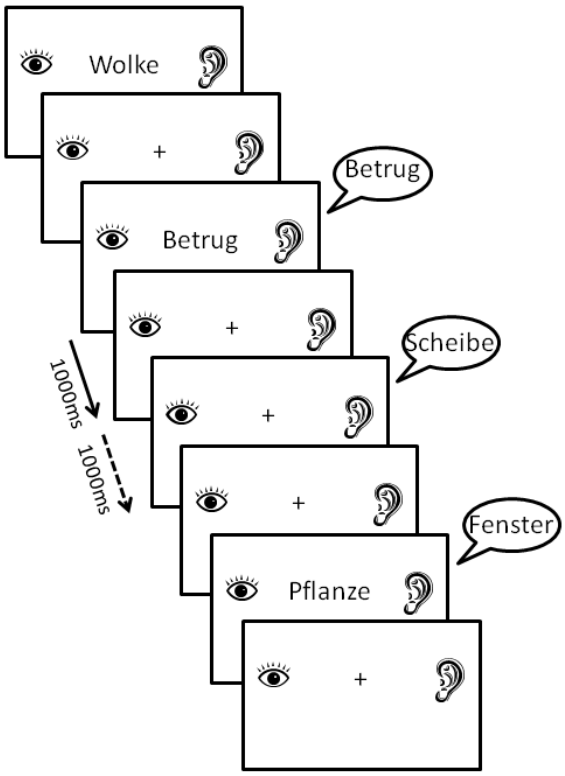

Figure 15 illustrates the **experimental design**. During the experiment were eighty disyllabic German nouns randomly presented either auditorily or visually alone or audiovisually simulaneously in a congruent or incongruent condition. Participants were asked to perform a discrimination task, by pressing two different mouse buttons. By unimodally presented signals they had to press the left and by bimodally presented stimuli they had to press the right mouse button.

The A stimuli were presented with a sound intensity of 70dB SPL and lasted about 800 ms while the V stimuli were presented for 1000 ms. The inter stimulus interval was approximately 1000 ms. All four conditions (A, V, AVc and AVi) were randomly presented by the presentation software (http://www.neurobs.com/) in four consecutive runs of approximately 3 minutes duration each. The participants performed a discrimination task and responded by press-

ing two different mouse buttons, in order to differentiate between the unimodal and bimodal signals that were presented. This task was performed to maintain the volunteers' attention during the experiment. The behavioral data of one non-dyslexic research participant was not recorded due to technical problems.

EEG Recording and Analysis

The EEG was continuously recorded from 29 channels and 2 zygomatic eye channels with a sampling rate of 500 Hz and a band pass filter (0-100 Hz) using an EEG-amplifier (Brainproducts, Munich, Germany). The silver/silver-chloride electrodes (Ag/AgCl) were located using the international 10-10 system: Fp1, Fp2, F7, F3, Fz, F4, F8, FT7, FC3, FC4, FT8, T7, C3, Cz, C4, T8, TP7, CP3, CPz, CP4, TP8, P7, P3, Pz, P4, P8, O1, Oz, O2. The reference electrode was placed at FCz. Two EOG electrodes were located below the outer cantus of each eye. During the EEG measurement the impedances were reduced below 5kΩ and the data was re-referenced offline to an average reference. Data analysis was performed utilizing the Brain Vision Analyzer software (Version 1.04, Brainproducts, Munich, Germany). In particular, the data was high- and low-pass filtered off-line at 1-30Hz. Eye-movement artifacts were removed using an independent component analysis (ICA) (Jung et al., 2000); further artifacts were erased by applying an automatic procedure (artifacts exceeding ±100µV were automatically rejected). The resulting data were segmented into 1100 ms epochs, baseline corrected relative to the -100 to 0 ms pre-stimulus time, and averaged for each participant and condition (A and V independently, as well as simultaneously presented either AVc or AVi). An average of the accumulated A and V presented stimuli and the AVc or AVi presented stimuli was calculated. Since, the super- or sub-additivity effect has been proposed as the principal mechanism for AV integration, the difference waves (DW) (AV-(A+V) for the AVc and AVi conditions were calculated on the single subject level. In addition, we calculated grand means of the DW for the AVc and the AVi conditions for both groups. The time segments for computing all statistical analyses were defined according to two consecutive global field power (GFP) minima (derived from all EEG channels) of the grand average of each group and condition (see Table 2). GFP was computed with the spatial root mean square method (RMS).

In the present study we analyzed GFP of the ERPs for each group and condition; this procedure permits the evaluation of the global brain activity elicited by AV, V or A word processing. GFP analysis can be considered as an established approach. Recently, Murray and colleagues have successfully demonstrated the application and benefits of the GFP procedure in the context auf AV integration (Murray et al., 2004).

Table 2: Time windows individually defined from the GFP for group and condition

Condition	Group	Time Window in ms	
DW incong	D	70	142
		142	252
		252	382
		382	620
	C	74	138
		138	254
		254	362
		362	580
DW cong	D	72	142
		142	252
		252	342
		342	516
	C	70	140
		140	246
		246	374
		374	644
auditory	D	90	170
		170	290
		290	332
		332	548
	C	90	172
		172	296
		296	446
		446	578
visual	D	48	142
		142	270
		270	404
		404	544
	C	50	130
		130	268
		268	416
		416	540

Legend 1: DW = Difference wave, incong = incongruent, cong = congruent

Additionally, in order to follow the dynamic time course of brain activation of AVc and AVi integration, a topographic analysis of variance (TANOVA) (Pascual-Marqui, Michel, & Lehmann, 1994) was applied to compare ERP maps obtained in the two groups. This procedure measures on a time-frame by time-frame basis differences between scalp potentials (i.e. maps, topographies). These statistical comparisons are carried out using the non-parametric rando-

mization methodology, which corrects for multiple testing (for a detailed description see (Strik, Fallgatter, Brandeis, & Pascual-Marqui, 1998)).

Results

Behavioral Data

During the experiment participants were instructed to discriminate between unimodally and bimodally presented words. This task was applied to ensure that participants maintained their attention during the entire experiment. The behavioral data were collected in form of response-accuracy (RA) and reaction time (RT) (see Figure 16).

Response Accuracy

Since the RA data collected during EEG-recording were not normally distributed according to the Kolmogorov-Smirnov-test, a non-parametrical procedure (Mann-Whitney U test) was applied. The outcome of this procedure revealed higher RA for non-dyslexic compared to dyslexic adults in both the unimodal (Mann-Whitney $Z=-2.419$, $p<0.01$, one tailed) and bimodal (Mann-Whitney $Z=-1.881$, $p=0.05$ one tailed) conditions.

Reaction Time

The RT data were normally distributed. Hence, we computed 4 x 2 ANOVA repeated measurements with four answer options (unimodal correctly; unimodal erroneously; bimodal correctly and bimodal erroneously judged signals) and two groups (dyslexic; non-dyslexic) as independent variables. This statistical procedure yielded neither significant main effects nor significant interactions. This result evidences no group differences in the RT.

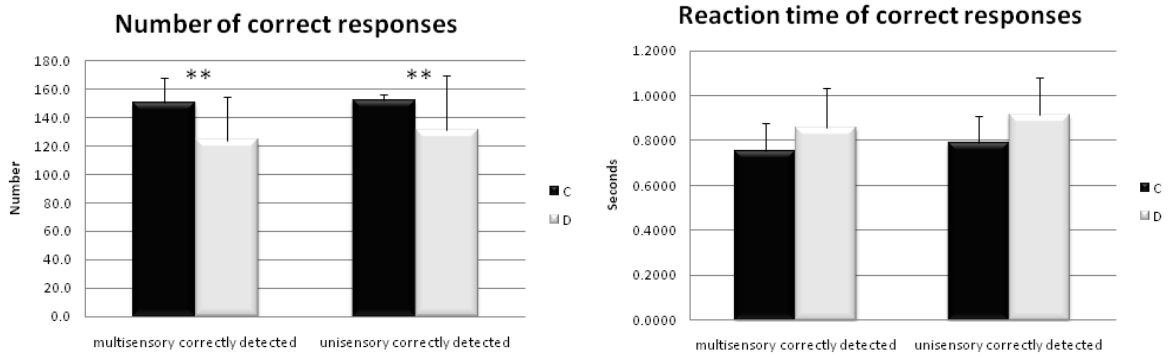

Figure 16 depicts the **behavioural data collected during the ERP experiment** for the dyslexic (light) and non-dyslexic/control (dark) participants. The first plot shows the percentage of correct responses for both groups during the unimodal and bimodal conditions. The second plot shows the reaction time for correctly identified trials for both groups. ** depicts significance, $p < .01$, and * illustrates significance, $p < .05$.

Analysis of the Audiovisual Integration Mechanism According to the GFP Values

As predicted by the super- or sub-additivity effect, AV integration occurs when AV > (A + V) or AV < (A + V). Therefore, integration during the AVc and AVi conditions was evaluated by comparing the summed A and V responses with those elicited by the AV signals. The mean GFP amplitudes of the difference waves (DW) (AVc -(A+V)) and (AVi -(A+V)) were applied, in order to evaluate activity over the whole scalp.

In order to examine the neurophysiological effects of AV integration variation as a function of group, we computed a 4 x 2 x 2 ANOVA with the between-subject factors: 4 TWs (N1/P1; P2/N2; P3; N4), 2 conditions (DW AVc; DW AVi) and within-subject factor: 2 groups (dyslexic; non-dyslexic). This analysis evidences that the AV integration differs significantly between the different TWs ($F(1,34)=150.498$, $p<0.001$), as well as between the different conditions ($F(1,34)=7.112$, $p<0.05$). Additionally, the same global ANOVA revealed a TW by group interaction ($F(1,34)=4.737$, $p<0.05$). This interaction indicates that the two groups integrated the AV presented words across the four different processing stages (TWs) in a different way.

In order to disentangle the TW effect that has been yielded by the global ANOVA, for every TW we calculated a separate 2 x 2 variance analysis (2 conditions as within-factor and 2 groups as between-factor). This computation yielded a main group effect ($F(1,34)=9.096$, $p<0.01$) for only the last TW that we examined. This result indicates that each of the two group's process audiovisually presented words in this TW differently.

Due to the fact that the global ANOVA revealed an additional main effect for condition, a 4 x 2 ANOVA for repeated measurements (4 TWs as within-factor and 2 groups as between-factor) was applied for the AVi and AVc condition. The result of the AVi condition indicates that the AV integration differs significantly during the various TWs ($F(1,34)=136.133$, $p<0.001$). A significant TW by groups interaction was found ($F(1,34)=5.056$, $p<0.05$) in the AVc condition.

In order to further elucidate the significant main group effect revealed in the latest TW, we examined post-hoc comparisons between conditions and groups. The Bonferroni corrected post hoc t-tests (two tailed) for independent samples revealed significant findings for the AVi ($t(34)=2.649$, $p<0.05$) and AVc ($t(34)=2.508$, $p<0.05$) conditions. This result indicates that the two groups process AV presented stimuli differently in a late deflection TW about 400 ms after stimulus onset (see Figure 17 & 18).

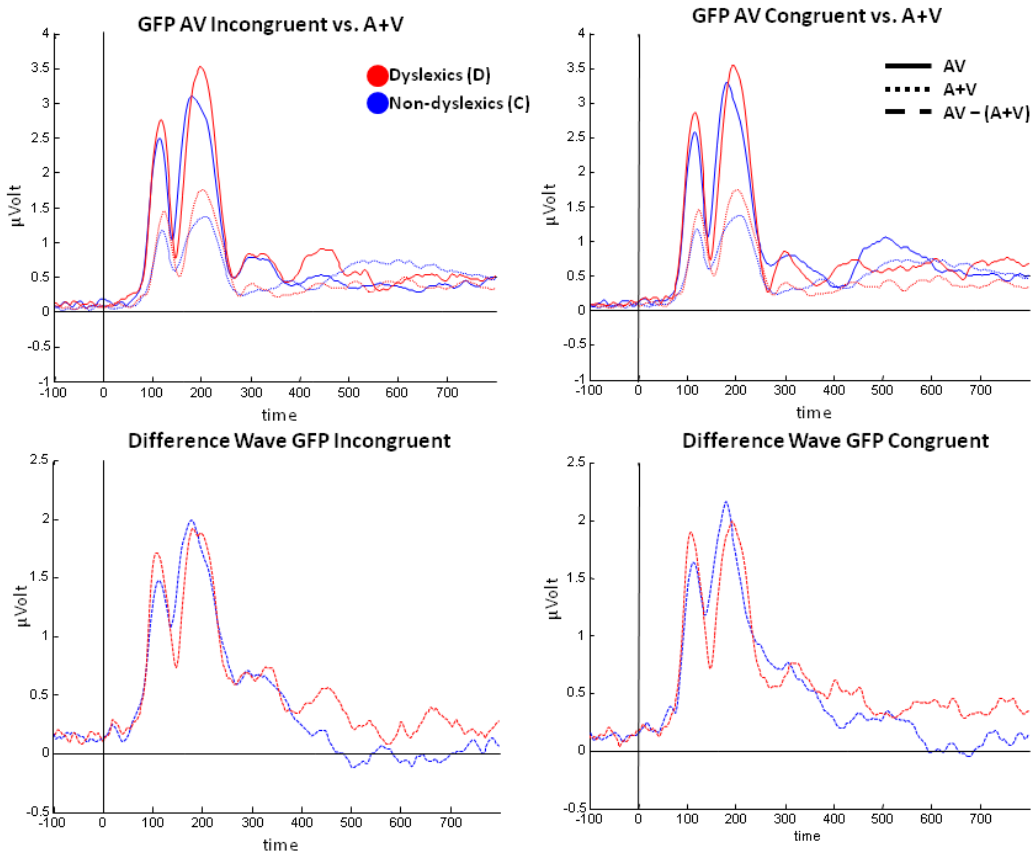

Figure 17 demonstrates the **mean amplitudes over the GFP for the AV congruent, AV incongruent and unimodal (A+V) condition**. Further, there are the difference waves AV-(A+V) for the congruent and incongruent conditions illustrated. The red line represents the dyslexic and the blue line the non-dyslexic individuals.

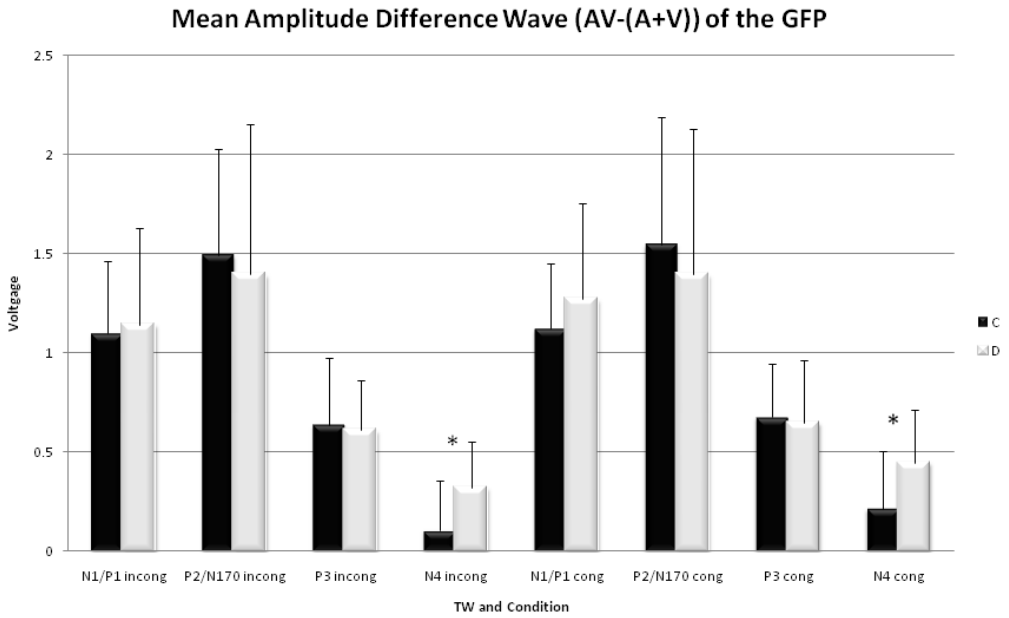

Figure 18 illustrates the **plots of the difference waves of the mean amplitudes over the GFP for the congruent (cong) and incongruent (con) conditions in four TWs (N1/P1; P2/N170; P3; N4)**. Dyslexic (D) (light bar) compared to non-dyslexic (C) (dark bar) adults show in the TW of the N4 component enhanced neuronal responses in both conditions. * depicts significance, $p < .05$.

Topographic Analyses:

To further explore the spatiotemporal pattern of brain responses derived from the two groups, we calculated a topographic analysis of variance (TANOVA) (Pascual-Marqui et al., 1994). This procedure detects topographic differences in the ERP maps that underpin the group differences of AV integration difference waves in late TWs (see Figure 19 & 20). Accordingly, the topographic maps of the DW yielded group differences in the congruent condition (AVc-(A+V)) between 448 ms and 486 ms ($p<0.05$). In the incongruent condition (AVi-(A+V) the topographic maps of the DW differed significantly between the groups from 408 ms to 432 ms ($p<0.05$) and from 462 ms to 550 ms ($p<0.05$) after stimulus onset.

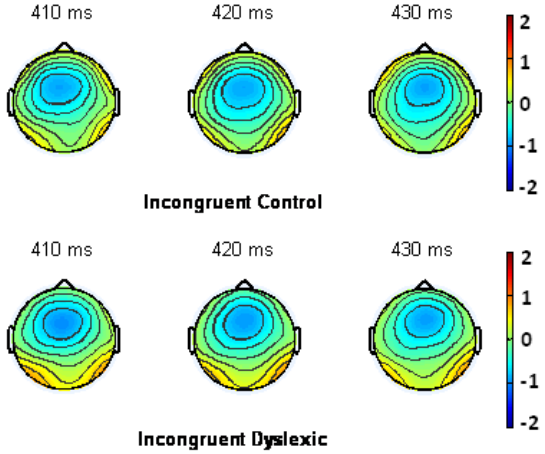

Figure 19 illustrates the **topographic maps of the difference waves over the TW from 390 – 430 ms** after stimulus onset for both groups and both conditions. Both conditions reveal in both groups typical topographic maps for the N400. The topographic maps from the incongruent condition differed significantly between the two groups from 408-432ms after stimulus onset. * illustrates significance, $p < .05$.

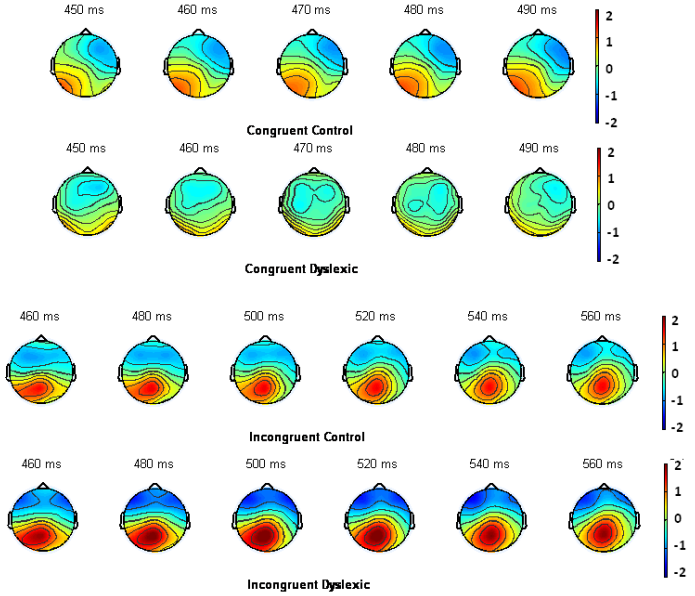

Figure 20 depicts the **topographic maps of the difference waves** for both conditions that differ significantly between the two groups. There was a significant group difference for the congruent condition from 448-490ms after stimulus onset and for the incongruent condition from 462-450ms after stimulus onset found.

Evaluating Incongruency Effects Between Groups

In a further step, we examined if the two groups differ in the AV processing of semantic information. Therefore, we investigated the incongruency effect between groups by analyzing the DW of the DW AVi[1] – DW AVc for the last TW examined in the present study. The t-test ($t_{(34)}$=0.322, p=0.75) we applied did not reveal a group difference. This indicates that the incongruency effect does not differ between groups.

Examine Unisensory Processing

In order to gain further insight into the unimodal processing modes and to evaluate if group differences during AV integration are caused by differential unimodal processing modes, we performed further analyses. These analyses involved a separate examination of either only visually, or auditorily presented stimuli.

To investigate the V domain, we computed a 4 x 2 ANOVA based on GFP values with the following independent variables: 4 TWs (N1/P1; P2/N2; P3; N4) and 2 groups (dyslexic; non-dyslexic). The outcome of this procedure yielded both a significant TW effect ($F_{(1,34)}$=11.522, p<0.01) and a significant interaction between group and TW ($F_{(1,34)}$=5.202, p<0.05). The post-hoc t-test revealed a significant group difference in the TW of the P2/N170 ($t_{(34)}$= 2.125, p<0.05) (see Figure 21).

In order to examine the A domain, a 4 x 2 variance analysis with 4 TWs (N1/P1; P2/N2; P3; N4) as within- and 2 groups (dyslexic; non-dyslexic) as between-subject factor was computed. This ANOVA revealed a main effect for TW ($F_{(1,34)}$=40.835, p<0.001).

[1] The DW AVc and DW AVi have been calculated for the analysis in the AV integration mechanism according to the GFP values.

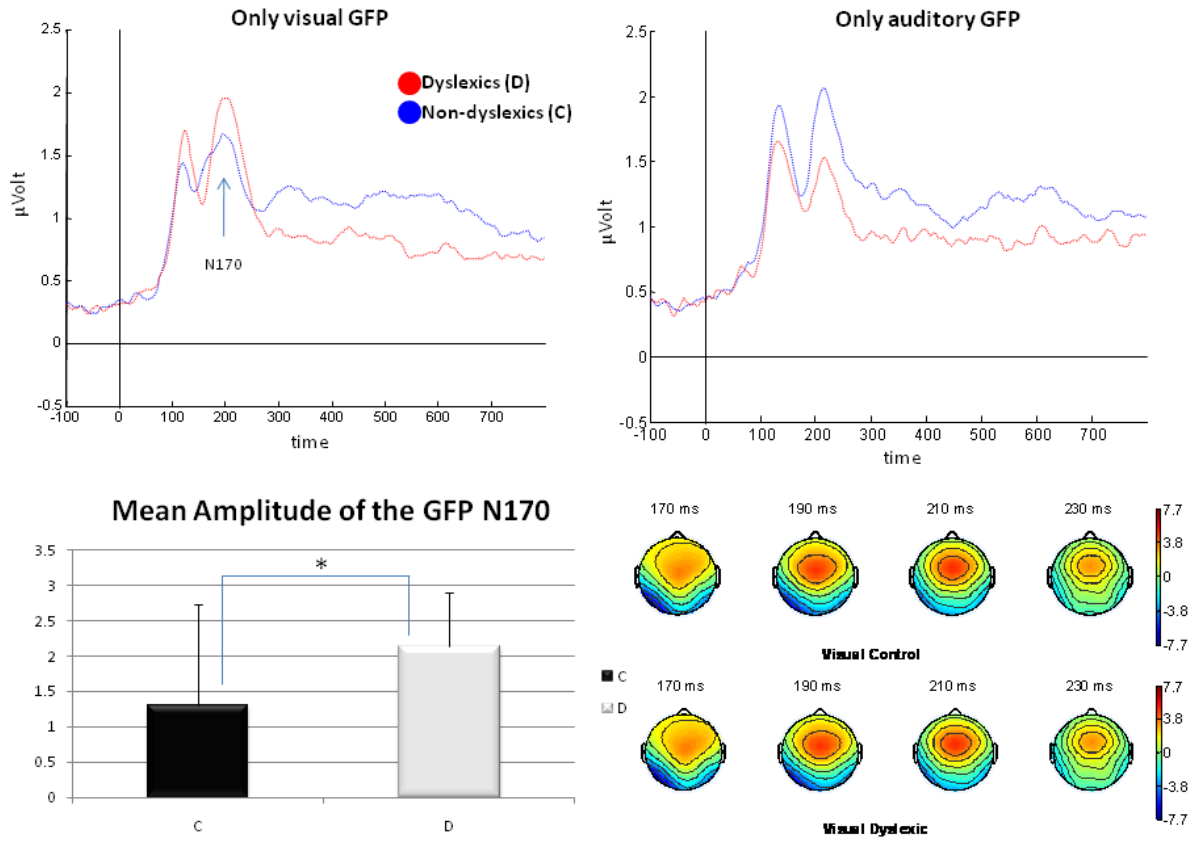

Figure 21 demonstrates the **mean amplitudes of the GFP for the visually and auditorily alone presented condition** for the dyslexic (red) and non-dyslexic (blue) adults. The plot on the lower left hand square shows the mean amplitudes of the GFP of the visual condition in the TW of the N170 for the dyslexic (D) (light bar) and non-dyslexic (C) (dark bar). * depicts significance, $p < .05$. In the lower left hand square are the topographic maps for the only visual condition in the TW of the N170 for both groups illustrated.

Discussion

This experiment was designed with the intention to characterize the time course and the neurophysiological correlates of AV integration while dyslexic and non-dyslexic individuals processed disyllabic words. This discussion consists of the following: First, we address behavioural data more comprehensively. Second, we discuss the EEG results that revealed AV integration in the late TW at around 400 ms. Third, we interpret the different processing patterns exhibited by the two groups in the visual domain.

Behavioral data

The behavioral data collected during the experiment revealed that the dyslexic as compared to non-dyslexic research participants had more difficulties in performing the perceptive discrimination task. In particular, the dyslexic adults committed more errors in the discrimination of uni- and bimodal signals. However, group differences for the reaction time measurements were not revealed. The reduced accuracy observed in dyslexic adults might be a result of at-

tention difficulties. In particular, we suggest that dyslexic individuals require more attention resources for processing stimuli with linguistic contents. Thus, it is possible that these subjects may have become tired; consequently, they made more errors.

EEG-Data:

Different Audiovisual Integration Between Dyslexic and Nondyslexic Adults

The main finding of our analyses is that dyslexic (vs. non-dyslexic) individuals consistently show magnified mean GFP amplitudes related to AV integration for both the AVc and AVi conditions in the last TW that we analysed (approximately 400 ms after stimulus onset). This indicates that dyslexic adults, as compared to non-dyslexic adults, recruit neuronal circuits differentially in response to AV presented linguistic stimuli. Thus, bimodal brain areas accountable for AV integration of language related information display differential responses in dyslexic compared to non-dyslexic individuals. To date the mechanisms underlying AV integration are not yet fully understood. It has been previously suggested that bimodal processing is advantageous when the unisensory domain is deprived. Hence, the pairing of weakly effective stimuli (those that are difficult to perceive or identify) results in a vigorous enhancement of the bimodal neuronal activity while the combination of highly effective stimuli causes little increase in the neural response. This mechanism is known as the inverse effectiveness rule (Calvert et al., 2004; Meredith & Stein, 1983). This theoretical framework posits that the increased neuronal response observed in dyslexic adults might reflect dysfunctional unisensory processing that leads to increased activation in bimodal areas. In accordance with the assumption of the feedforward mechanism in AV integration (Driver et al., 2008), we posit that the enhanced N170, which we observed during the visual condition in dyslexic (vs. non-dyslexic adults) could modulate the AV processing in a later TW.

A further theoretical framework that may be helpful when interpreting the dysfunctional bimodal processing observed in dyslexic adults is the neuronal efficiency hypothesis (NEH). This framework predicts that lower and more focused cortical activation reflects higher neural efficiency (Micheloyannis et al., 2006) and preferentially occurs in experts. The proponents of NEH emphasize the crucial (and sufficient) role of extensive and elaborated knowledge, which is often the result of more than a decade's experience and intensive practice in the respective domain (Ericsson & Smith, 1991). The neuronal underpinnings of the NEH theory regarding experts are, for example, supported in studies examining multimodal integration in elite karate athletes. A reduced cortical activation was revealed in athletes compared to non-athletes either performing a visuo-motor task related to their field of expertise (Del Percio et

al., 2008), or during voluntary self-paced right finger movements performed in the absence of visual stimuli (Di Russo, Pitzalis, Aprile, & Spinelli, 2005; Kita, Mori, & Nara, 2001). Similarly, non-dyslexic individuals are characterized by more proficiency in word decoding and spelling abilities in comparison to dyslexics. Therefore, skilled readers process phonological information more efficiently whilst recruiting a smaller neuronal network.

The electrophysiological responses revealed in the last TW that we analysed (approximately 400 ms after stimulus onset) are interpreted as specific language-related functions, which reflect the AV integration of semantic information. Processing semantics in linguistic contexts is associated with the N400 component (Kutas & Hillyard, 1980). The amplitude of the N400 varies systematically with semantic congruence. Thus, this component is dependent on the immediate context in which it occurs, for example, by reading a sentence or single words. Additionally, the N400 has also been implicated in semantic mismatch processing of object stimuli (Kutas & Federmeier, 2000). Previous studies investigating the integration of AVc and AVi object-related stimuli have revealed an AV incongruency effect. This effect resulted in a more negatively directed ERP response, which occurred at approximately 400 ms after the stimulus onset (Molholm, Ritter, Javitt, & Foxe, 2004). In addition, further evidence provided by a previous MEG study supports the argument that AV integration is associated with the processing stage reflected by the N400 component (Raij et al., 2000). These authors investigated the matching and non-matching effects of visual- and auditory-presented letters and found differential interactions in the left and right hemisphere after stimulus onset. This evidence overlaps with the time course of the N400 (Raij et al., 2000). The incongruency effect did not differ between groups in our research study. However, our topographic maps of the congruent and incongruent condition showed a typical N400 effect, which was reflected in a central negativity. Notably, our data evidenced group differences as illustrated by the topographic maps associated with the AVi condition from 408 ms to 432 ms after stimulus onset. This finding might reflect a different proficiency to integrate semantic information between dyslexic and non-dyslexic individuals. Due to an intact phonological system of non-dyslexic adults, words might be better represented in the orthographical lexicon whereas dyslexic adults might show less sensitivity to this kind of semantic violation. This reasoning is in line with the phonological deficit theory (Bradley et al., 1983; Ramus et al., 2003b). In addition, our investigation revealed group differences in the topographic maps for both AVc and AVi conditions in late TWs. In particular, our results suggest a divergent scalp distribution between the two groups for the AVc condition from 448 to 486 ms after stimulus onset and for the AVi condition from 462 to 550 ms after stimulus onset. These supplementary findings

indicate that AV presented nouns are processed differently between the two groups especially in late TWs. Additionally, these results support the phonological processing theory that dyslexic individuals have impairments in higher cognitive functions, such as, representation, storage and/or retrieval of linguistic material. This impairment might be a result of reading and spelling difficulties experienced during childhood.

Group Gifferences in the Processing of Only Visually Presented Stimuli

Our findings of enhanced response in the TW, which overlap with the elicitation of N170 in response to visual presentation in dyslexic compared to non-dyslexic adults, deserve a brief discussion. The N170 component elicited over left occipito-temporal regions has previously been associated with expertise for word-forms and letter strings (Bentin et al., 1999; Nobre et al., 1994). Although the N170 component in non-reading kindergarten children was absent, it emerged less than two years later as the same children had mastered basic reading skills in 2nd grade (Maurer et al., 2006). In children approximately 10 years of age, the N170 was elicited bilaterally over occipito-temporal areas during word and pseudoword reading; however, it was elicited to a lesser extent in dyslexic children (Kast, Elmer, Jancke, & Meyer, 2010). Whereas skilled adult readers show increased activity over the leftward occiptio-temporal regions (McCandliss et al., 2003b), dyslexic adults process word-forms bilaterally (Helenius et al., 1999). Meanwhile, it has been established that neuronal reorganization is integral to the process by which reading experience drives the progressive specialization of a pre-existing inferior temporal pathway that is dedicated to visual object recognition (Brem et al., 2006; McCandliss et al., 2003b; Polk et al., 2002).

Accordingly, we interpret the enhanced mean amplitude of the GFP, which occurs in a TW sensitive component for processing print in dyslexic adults (vs. non-dyslexic adults), as a means to compensate for their reduced neuronal responses over posterior sites. Hence, we assume that dyslexic compared to non-dyslexic adults recruit a larger and wider neuronal network, in order to perform the phoneme to grapheme mapping essential for word decoding. Therefore, we suggest that the reduced proficiency in phoneme to grapheme mapping skills and word decoding comply with the NEH theory as is evidenced by stronger electrophysiological responses over the global brain.

We identified group differences in a TW sensitive for phoneme to grapheme mapping in the V, but not in the AV processing mode. This suggests that the impaired phoneme to grapheme mapping concept, as postulated by the phonological deficit theory, only occurs during the V,

and not the AV condition. We argue that dyslexic adults have been able to compensate for this deficit, which is linked to the visual domain, by strengthening the auditory pathway. Alternatively, two previous fMRI studies have revealed different AV processing modes in dyslexic adults (Blau et al., 2009) and dyslexic children (Blau et al., 2010), as compared to non-affected individuals, during the performance of a letter to sound mapping task. Perhaps it is because of the stimulus material used in our study that no group differences during the processing stage in the AV conditions were found. Whereas the previously mentioned fMRI studies (Blau et al., 2009; Blau et al., 2010) used phonemes and letters, we investigated the processing of disyllabic words. The dual route theory (Coltheart et al., 2001) maintains that previously encountered words are stored in the orthographical lexicon. Thus, words are recognized very quickly while pseudowords are processed by the indirect route and must be decoded more segmentally (grapheme has to be matched to the corresponding phoneme) (Jobard et al., 2003).

Despite the novel findings we reported in the present work, further investigations are needed, in order to clarify the differential AV processes revealed in dyslexic (vs. non-dyslexic individuals). Since pseudowords are processed by the grapho-phonological route, it would be interesting to examine the AV processing of pseudowords. Additionally, it would be intriguing to compare dyslexic versus non-dyslexic children who exhibit less strengthened phoneme to grapheme mapping.

Conclusion

This novel study focussed on the AV integration of disyllabic words in dyslexic and non-dyslexic adults. We uncovered enhanced mean amplitudes in dyslexic adults for both the AVc and AVi integration conditions. These findings indicate that neural mechanisms, which subserve multimodal word processing differ between dyslexics and non-dyslexics.

Moreover, we discovered that visually presented words resulted in enhanced mean amplitudes for the dyslexic adults compared to non-dyslexic adults; this may reflect the impairment of phoneme to grapheme mapping. However, this finding was absent in the AV condition. Hence, we assume that the impairment in the visual modality might be compensated by the enhanced incorporation of auditory information during AV processing.

Acknowledgment

This project was supported by the Research Funding University of Zurich (56234102), SNF-grant nr. 320000 – 120661/1 and SNF, grant nr. 31003A-100109.

8.3 Experiment III: Multi- and Unisensory Decoding of Words and Nonwords Result in Differential Brain Responses in Dyslexic and Nondyslexic Adults

Monika Kast[1], Ladina Bezzola[1], Lutz Jäncke[1] & Martin Meyer[1]

[1]Department of Neuropsychology, University of Zurich, Switzerland

Abstract

The present functional magnetic resonance imaging (fMRI) study was designed to investigate the neural substrates involved in the audiovisual processing of disyllabic German words and pseudowords. Twelve dyslexic and 13 non-dyslexic adults performed a lexical decision task while stimuli were either presented unimodally (either aurally or visually) or bimodally (audiovisually simultaneously).

The behavioral data collected during the experiment evidenced more accurate processing for bimodally than for unimodally presented stimuli irrespective of group. Words compared to pseudowords were processed faster in terms of behavioral responses. Notably, no group differences have been found for either accuracy or for reaction times. With respect to brain responses non-dyslexic compared to dyslexic adults elicited stronger hemodynamic responses in the leftward supramarginal gyrus (SMG), as well as in the right hemispheric superior temporal sulcus (STS). Additionally, our data yielded a group by modality interaction in the rightward insula. Dyslexic compared to non-dyslexic adults showed reduced responses to only aurally presented signals and enhanced hemodynamic responses to audiovisual, as well as visual stimulation.

Our behavioral data results evidence that the two-syllabic nouns were easy to identify for both groups. In contrast, our analysis revealed hemodynamic differences between groups, especially in heteromodal areas. This finding indicates that dyslexics show less neuronal involvement in audiovisual integration regions, namely, the STS, SMG and insula when decoding phonological information. We posit that these impaired multimodal neuronal circuits cause difficulties to efficient and reliable phoneme to grapheme mapping that is essential for word decoding.

Introduction

Phonological Deficit in Developmental Dyslexia

Developmental dyslexia is characterized by low reading and spelling skills in spite of an average IQ, conventional education, and solid social background (World Health Organization, 1993). The causes of spelling and reading failure are still debated. There exist several theories, which focus on the general auditory (Baldeweg et al., 1999; Tallal, 1980; Tallal & Gaab, 2006), visual (Livingstone et al., 1988; Lovegrove et al., 1980; Stein et al., 1997), auditory and visual (Farmer et al., 1995), or motor impairments (Nicolson et al., 1990; Rudel, 1985; Wolff et al., 1990) that dyslexic individuals often suffer from. One of the most agreed theories is the phonological processing deficit hypothesis (Bradley et al., 1983; Ramus et al., 2003b). This theory suggests a specific impairment in the representation, storage and/or retrieval of speech sounds (Bradley et al., 1983; Ramus et al., 2003b), as well as a reduced development of the appreciation for the segmental nature of speech, resulting in limited phonological awareness (Frith, 1985). This notion is manifested in impaired phoneme to grapheme mapping skills. Accordingly, letters and speech sounds are the basic elements of correspondence between written and spoken language. The establishment of culturally defined associations between visual (grapheme) and auditory (phonemes) representations are fundamental for acquiring written-word decoding skills (Byrne, 1998). The grapheme to phoneme association, which is pertinent to reading relies on proper audiovisual (AV) processing mechanisms that are similar to the AV integration of speech (Raij et al., 2000; van Atteveldt et al., 2004). The notion of an AV mechanism that is essential for decoding written content, leads to the suggestion that the phonological deficit of dyslexic individuals may be reflected in an impaired AV processing of phonological information.

Audiovisual Processing

To date, the underlying mechanisms of AV integration, which is necessary for word decoding, are not completely understood (Molholm et al., 2002). Previous studies have demonstrated that neurons in the primary sensory areas preferentially respond to stimuli in one sensory modality. In contrast, neurons in multisensory association areas like the inferior parietal lobe (IPL), superior temporal sulcus (STS) (Thompson et al., 1963), middle temporal gyri (Seltzer & Pandya, 1994) as well as insula (Bamiou et al., 2003) have been identified to respond specifically to the combinations of different modalities, such as audiovisual stimuli (Benevento et al., 1977). Multisensory integration occurs when information of two or even more sensory

systems derive in close temporal and spatial proximity. The observed facilitation of the neuronal response is often maximal when the response to the individual inputs is weak. This principle is known as inverse effectiveness (Calvert et al., 2004).
The fact that responses from one modality can influence the neural mapping of another modality and information from different modalities interact with each other, leads to the suggestion that the subtle coding deficits in the auditory and visual domains observed in dyslexic individuals might influence the processing or multimodal information. Alternatively, it might be that the development in one modality guides the successful development in other modalities (Pammer & Vidyasagar, 2005). Reading requires the synchronicity of both auditory and visual information. Thus, a slight developmental impairment in one modality may result in concomitant impairment in the other modality. Therefore, this multimodal impairment may manifest in decoding problems, such as phonological processing deficits and/or visual coding difficulties (Pammer et al., 2005).

Theoretical Framework of Word Decoding

To date, the underlying mechanisms of AV integration that are necessary for word decoding are not completely understood (Molholm et al., 2002). Previous studies have demonstrated that neurons in the primary sensory areas preferentially respond to stimuli in one sensory modality. In contrast, neurons in multisensory association areas, such as, the inferior parietal lobe (IPL), superior temporal sulcus (STS) (Thompson et al., 1963), middle temporal gyri (Seltzer et al., 1994), as well as insula (Bamiou et al., 2003) have been identified to respond specifically to the combination of various modalities, such as audiovisual stimuli (Benevento et al., 1977; Ghazanfar & Schroeder, 2006). Multisensory integration occurs when the information of two or more sensory systems takes place in close temporal and spatial proximity. This co-incidence can yield as an advantage. This observed facilitation of the neuronal response is often maximal if the response to the individual input is weak. This principle is known as inverse effectiveness (Calvert et al., 2004).
Since responses from one modality can influence the neural mapping of another modality, and information from different modalities interact with each other, subtle coding deficits in the auditory and visual domains that have been observed in dyslexic individuals might influence the processing or multimodal information. Alternatively, it might be that the development in one modality guides the successful development in other modalities (Pammer et al., 2005). Reading requires the synchronicity of both auditory and visual information. Thus, a slight developmental impairment in one modality may result in a concomitant impairment in another

modality. Therefore, this multimodal impairment may become manifest in decoding problems, such as, phonological processing deficits and/or visual coding difficulties (Pammer et al., 2005). The integrity of multisensory supporting phonological functions become evident at the level of word decoding.

Theoretical Framework of Word Decoding

According to the theoretical framework of the dual route theory (Coltheart et al., 1993; Coltheart et al., 2001) decoding of words should be achieved through two distinct routes that mediate two alternative processes. One is the grapho-phonological pathway, also called the indirect route, and it requires visual words to be transformed into their auditory equivalent. This happens when a grapheme is mapped onto its equivalent phoneme. This grapheme to phoneme correspondence is a prerequisite for accessing meaning. Newly encountered words or pseudowords are processed by the grapho-phonological route (Jobard et al., 2003). The second pathway is the lexico-semantic, or direct route. This process relies on the direct association between the visual form of words and their meaning. This association is thought to build progressively when subjects repeatedly encounter and learn words. Therefore, learned word forms are stored in long-term memory in a visual word form system, also called the orthographical lexicon (Coltheart et al., 2001).

Aim of the Present Study

The current fMRI study was designed, in order to examine the neuronal correlates of processing words and pseudowords aurally (A), visually (V) and audiovisually (AV) in dyslexic and non-dyslexic adults. There exists a multitude of explanations describing the deficient mechanisms underlying developmental dyslexia since this disorder shows a wide range of heterogeneous symptoms. To date, researchers investigating dyslexia have mainly focused on the neuronal underpinnings of phonological information in unisensory (i.e. auditory, visual) domains. In contrast, by means of the present work, we aim to examine the AV processing of linguistic material and investigate group differences. We maintain that decoding written words and pseudowords requires the coding of orthographic information into the phonological representation. Aurally (A) presented words must be segmented into smaller units (phonemes) and these phonemes should then be associated with a meaning. According to the dual route theory, however, previously encountered words are stored in the orthographical lexicon and are processed by the direct route. In contrast, pseudowords have to be processed by the grapho-phonological pathway wherby phoneme to grapheme mapping is more explicitly in-

volved. Since an efficient association of phonemes to graphemes is essential for word and in particular pseudoword decoding, the present work was designed, to contribute to a better understanding of audiovisual processing of phonological information in dyslexic and non-dyslexic adults. Nevertheless, since this study has an innovative character. We are unable to predict whether incompetent audiovisual word decoding results in diminished or enhanced neuronal responses in dyslexic adults.

Previous fMRI studies, which investigated the unimodal (V, A) and bimodal (AV congruent or AV incongruent) letter-speech sound associations in both dyslexics and non-dyslexics, have revealed lower activation levels in the bilateral superior temporal cortex during the integration of letters and speech sounds for dyslexic as compared to non-dyslexic adults (Blau et al., 2009). Furthermore, dyslexic compared to non-dyslexic children showed reduced neural integration in the bilateral auditory areas, namely, the planum temporale and Heschl's sulcus, as well as the STS (Blau et al., 2010). Accordingly, we predict that we will observe group differences in a typical AV integration area, such as, the STS. Our hypothesis is that non-dyslexic, compared to dyslexic adults will show enhanced responses in the vicinity of the left STS. Additionally, it is known that the left parietal cortex receives multimodal sensory inputs (Pourtois & de Gelder, 2002) and plays an important role in the integration of multimodal synthesis of spatial information (Farah, Wong, Monheit, & Morrow, 1989). We assume that the integration of multimodal (i.e. AV) and spatial information are essential for reading since each grapheme must be performed at the correct place and in the order to the corresponding phoneme. Therefore, we also predict group differences in the inferior parietal lobe, in terms of impaired phoneme to grapheme mapping skills in dyslexic individuals. Additionally, we assume that non-dyslexic compared to dyslexic adults process the words and pseudowords more accurately and efficiently.

Methods

Participants

Twelve dyslexic (D) adult individuals (26.1 ± 6.3 SD years of age, 3 female and 9 male, 11 right and 1 left handed) and 13 non-dyslexic (C) adults (26.3 ± 3.0 SD years of age, 3 female and 10 male, 13 right handed) participated in the present study. The two groups (D, C) did not significantly differ in age ($t_{(23)}$=-0.083, p=0.934). Their handedness was assessed by the Annett questionnaire (Annett, 1970). Dyslexic individuals were referred to our study by their therapists, as well as by flyers distributed in technical colleagues and at several universities.

For all of the dyslexic subjects, their respective diagnosis had been established in elementary school. In a standardized spelling test based on the German language "Rechtschreibungstest" for adults (Kersting et al., 2004) dyslexic adults achieved 15.15 (±18.13) percent; non-dyslexic individuals attained 58.61 (±16.37) percent; non-dyslexic compared to dyslexic individuals performed significantly better ($t_{(23)}$=6.23, p<0.001). Seven of the dyslexic individuals had received an academic education. Five of the dyslexic participants had completed an apprenticeship. In the non-dyslexic group, 12 adults underwent an academic education, and one a non-academic education with an apprenticeship. The average years of school completed were 14.96 in the dyslexic group and 15.42 in the non-dyslexic group. Thus, the two groups did not differ significantly in their number of school years ($t_{(23)}$=-0.413, p=0.684). All participants were native Swiss-German or German speakers, had no history of neurological or psychiatric disorders, normal to corrected-to-normal vision, and reported normal hearing. All participants gave written consent. This study has been approved by the local ethics committee (SPUK), in accordance with the declaration of Helsinki.

Pre-scanning Training

Before applying the fMRI protocol, each subject performed a lexical decision task outside the scanner that included words and pseudowords. This procedure was applied to ensure that 1000 ms stimulus presentation was long enough to be decoded for dyslexic individuals and for subjects to become familiar with the task. This pre-experiment comprised 10 disyllabic nouns consisting of five letters and 10 disyllabic pseudowords (consisting of the same letters as the nouns). The 20 stimuli were presented randomly for 1000 ms with an inter stimulus interval (ISI) of 3000 ms by the presentation software (www.neurobs.com).

Stimuli and Task Design

In the scanner, the participants performed a lexical decision task consisting of words and pseudowords. Each participant was requested to make a button response as accurately and as quickly as possible. The words were disyllabic abstract German nouns or concrete German words (W) (e.g. "Lehre" *apprenticeship*); pseudowords (PW) consisted of the same five letters as the nouns (e.g. "Herle"). The stimuli were randomly presented either aurally (A) or visually (V) alone, or simultaneously (AV) by the presentation software (www.neurobs.com) (see Figure 22). The auditory stimuli were presented via headphone specifically designed for MR-environment. The visual stimuli were projected onto a translucent screen that participants viewed inside the scanner via a mirror. The stimuli presentation lasted 1000 ms; the stimuli

were systematically jittered with an ISI varying from 10 000 to 14 000 ms. Participants were instructed to keep their eyes open during stimulus presentation and to focus on the fixation cross presented on a screen during ISI. A fixation cross appeared on the screen once the visually presented stimulus disappeared; thus, the fixation cross was also visible during the presentation of empty trials. The experiment consisted of four runs with 30 trials for each condition (30 x 6 conditions = 180 trails) with at least 60 empty trails. The total scanning time lasted approximately 50 minutes.

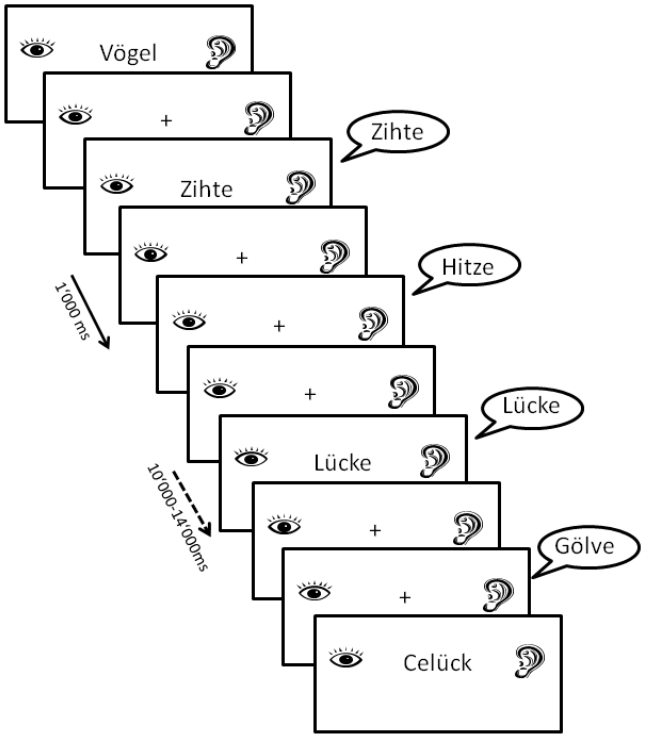

Figure 22 demonstrates the experimental design. Words and pseudowords were either presented unimodally (auditorily or visually) or audiovisually. The stimulus presentation lasted 1 second and the stimulus onset asymmetry (SOA) took place between 10 to 14 seconds. The data acquisition was split in three runs, whereas one run lasted approximately 12 minutes.

fMRI Data Acquisition and Analysis of Imaging Data

A Philips Intera 3T whole-body MR unit (Philips Medical Systems, Best, The Netherlands) equipped with an eight-channel Philips SENSE head coil was used to acquire magnetic resonance images. Functional images of the whole brain were acquired by 299 whole-head scans per run (1196 for 4 runs) using a Sensitivity Encoded (SENSE) (Pruessmann, Weiger, Scheidegger, & Boesiger, 1999) single-shot echoplanar imaging technique (repetition time (TR) = 2500ms , echo time (TE) = 35 ms, flip angle = 78°, field of view (FOV) = 220 mm x 164 mm x 220 mm, acquisition matrix = 80 x 80, voxel size = 2.75 x 2.75 x 4 mm; slice thickness = 4 mm; interslice gap = 0 mm).

Analysis of Imaging Data

Preprocessing and MRI data analysis were performed using MATLAB 2008a (Mathworks Inc., Natick, MA, USA), and SPM5 software package (Institute of Neurology, London, UK). All images were realigned to the first recorded volume per run, normalized into standard stereotactical space (using the EPI-template provided by the Montreal Neurological Institute, MNI brain), interpolated to a voxel size of 2.0 x 2.0 x 2.0 mm, and spatially smoothed using a 8 mm full-with-at-half-maximum (FWHM) Gaussian kernel. Activated voxels were identified by the general linear model approach (Friston et al., 1995), which had been implemented in SPM5. During the first level of analysis, a statistical model with separate regressors for the response phase was individually computed for each subject (modeled as epochs of 1 second). This model included six regressors (A W, A PW, V W, V PW, AV W, AV PW). A high pass filter with a cut-off of 128 seconds was applied. After model estimation, linear contrasts were calculated for the six conditions.

For the group level analysis, we specified a 3 x 2 x 2 factorial design (SPM5) with the with-in factors modality (A, V, AV), and stimuli (W, PW), and the between factor group (D, C). To disentangle the main effects for group, modality and stimuli, as well as to disentangle significant interactions, we performed post-hoc ROI-analyses using spheres of 4 mm radius centered at maximal local F-values (Bosch, 2000). For this procedure, we used the freeware marsbar (http://marsbar.sourceforge.net/). Mean BETA values were deduced by in-house programmed MATLAB (http://www.mathworks.com/) scripts and further analyzed by means of *t*-tests (SPSS, http://www.spss.com/).

In order to calculate the positive and negative correlations between spelling skills, i.e. results from “Rechtschreibungstest”, with the hemodynamic response for the different modalities and stimuli, we applied multiple regressions implemented in SPM 5.

Results

Behavioral Performance:

Pre-experiment

The behavioral data of the pre-experiment were not normally distributed according to the Kolmogorov-Smirnov-test; thus, a non-parametrical procedure (Mann-Whitney U test) was applied. There were no group differences revealed for accuracy in correctly detected PW

(Mann-Whitney Z= -0.598, p=0.598) and correctly detected W (Mann-Whitney Z= -0.555, p=0.579), or for reaction time in correctly detected PW (Mann-Whitney Z= -0.979, p=0.328) and in correctly detected W (Mann-Whitney Z= -0.163, p=0.87).

Experiment: Accuracy

The behavioral data for accuracy, which were collected during the fMRI experiment were analyzed by applying a 3 x 2 x 2 ANOVA for repeated measurements with the independent variables modality (A, AV, V), stimuli (W, PW), and group (D, C). The outcome of this procedure (see Figure 23) revealed a main effect modality ($F_{(1,23)}$=43.249, p<0.001) and a significant interaction for modality by group ($F_{(1,23)}$=4.598, p=0.043). In order to explore the significant modality effect, two 3 x 2 ANOVAS for repeated measurements were separately calculated for W and PW. For W, the analysis demonstrated a main effect modality ($F_{(1,23)}$=40.548, p<0.001) and a significant modality by group interaction ($F_{(1,23)}$=6.778, p=0.016). For PW, a main effect modality ($F_{(1,23)}$=20.489, p<0.001) was found.

Independent of group and lexicality the post-hoc t-test (two tailed) revealed that bimodally presented words and pseudowords are more accurately processed than unimodally presented stimuli. Significant differences were revealed for pseudowords between A and AV ($t_{(24)}$=-4.562, p<0.001), and V and AV ($t_{(24)}$=-2.5, p=0.02). For words we found significant differences between A and AV ($t_{(24)}$=-4.11, p<0.001), and V and AV ($t_{(24)}$=-2.522, p=0.019)).

Experiment: Reaction Time

The reaction times collected during the fMRI experiment were analyzed by applying a 3 x 2 x 2 ANOVA for repeated measurements with modality (A, AV, V) and stimuli (W, PW) as within-subject factors and group (D, C) as between-subject factor. This analysis yielded a main effect for the factor modality ($F_{(1,23)}$=113.737, p<0.001) and for stimuli ($F_{(1,23)}$=25.685, p<0.001). In order to examine the main effect modality, two 3 x 2 ANOVAs for repeated measurements were separately calculated for W and PW. The outcome of this procedure revealed a main effect modality for W ($F_{(1,23)}$=111.701, p<0.001) and PW ($F_{(1,23)}$=68.994, p<0.001). The post-hoc t-test (two tailed) yielded significant differences between A and AV ($t_{(24)}$=11.77, p<0.001), as well as between A and V ($t_{(24)}$=10.659, p<0.001) for words. Additionally, our analysis revealed significant differences between A and AV ($t_{(24)}$=11.367, p<0.001), as well as between A and V ($t_{(24)}$=7.923, p<0.001) for presented PW.

To onward the investigation in reaction time of the effect for stimuli yielded by the main ANOVA three separate variance analyses were applied for the A, AV and V modalities.

These analyses yielded a main effect stimuli for the A ($F_{(1,23)}$=15.153, p<0.001), AV ($F_{(1,23)}$=29.613, p<0.001) and V ($F_{(1,23)}$=14.826, p<0.001) modalities. The post-hoc t-tests (two tailed) revealed significant differences between W and PW for the A ($t_{(24)}$=3.982, p=0.001), AV ($t_{(24)}$=5.35, p<0.001), and V ($t_{(24)}$=3.832, p=0.001) modalities.

In sum, words are generally processed faster than pseudowords irrespective of group. The longest reaction times were found for aurally presented stimuli.

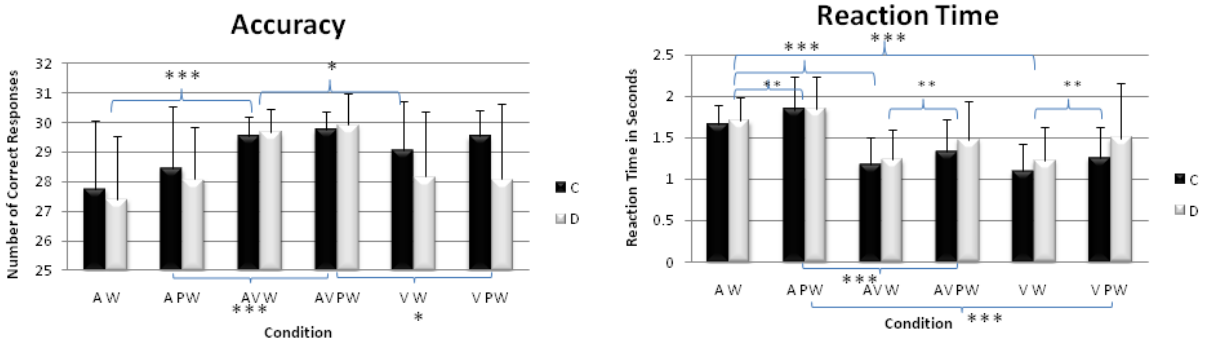

Figure 23 depicts the behavioral data for accuracy and reaction time collected during the fMRI experiment. The plots illustrate auditorily (A), audiovisually (AV) and visually (V) presented words (W) and pseudowords (PW) for the non-dyslexic (dark bar) and dyslexic (light bar) adults. * illustrates significance, p<0.05, ** demonstrates significance, p<0.01 and ***shows significance, p<0.001.

Contrasts Between Groups in Turns of Audiovisual Stimulation

In order to investigate the network involved during AV stimulation, we computed the combined W and PW contrasts between dyslexic and non-dyslexic adults. We applied this procedure in both directions, dyslexic vs. non-dyslexic and vice versa. These data are illustrated in Table 3. Only significant clusters of activation were considered (uncorrected α-level 0.001, k ≥ 30, non-isotropic correction).

Brain Activation Related to Condition, Stimuli and Group

In order to uncover main effects of brain activity, we performed a 3 x 2 x 2 full factorial design (SPM5) with the within-factors modalities (A, AV, V), and stimuli (PW, W), and the between-factor group (D, C). Only significant clusters of activation were considered (uncorrected α-level 0.001, k ≥ 30, non-isotropic correction). All significant clusters representing main effects and interactions are listed in Table 4.

Table 3: Contrasts of audiovisual activation pseudoword and word

Contrast	**Anatomical structure**			**Coordinates**					
Pseudoword & Word	**Region**	**Direction**	**Side**	**x**	**y**	**z**	**Cluster size**	**T-value**	**p-vlaue**
Controls (C) vs Dyslexics (D)								T(48)	
	Inferior Parietal	C > D	L	-52	-44	36	88	4.38	<0.001 uncor
	Precuneus	C > D	L	-12	-60	46	45	3.91	<0.001 uncor
	Angular	C > D	L	-36	-60	30	30	3.67	<0.001 uncor
	Middle occipital	C > D	R	32	80	36	135	5.47	<0.001 uncor
	Precuneus	C > D	R	18	-66	40	144	4.73	<0.001 uncor
	Middle Temporal	C > D	R	56	-18	-12	32	4.36	<0.001 uncor
	Angular	C > D	R	34	-64	44	31	4.22	<0.001 uncor
	Outside Angular	C > D	R	36	-48	32	75	3.99	<0.001 uncor
Dyslexics (D) vs Controls (C)									
	Insula	D > C	L	-42	16	-2	36	4.39	<0.001 uncor
	Precentral	D > C	L	-34	4	30	21	4.35	<0.001 uncor
	Mid cingulum	D > C	L	-6	10	36	58	3.90	<0.001 uncor
	Lingual Gyrus	D > C	L	-14	-46	0	32	3.68	<0.001 uncor
	Insula	D > C	R	36	22	0	65	4.38	<0.001 uncor
	Mid cingulum	D > C	R	6	18	30	76	4.13	<0.001 uncor
	Outside Precentral	D > C	R	28	-8	42	76	4.09	<0.001 uncor

Table 4: Location of activation peaks for main results of the 2x2x3 ANOVA

Main effect	**Anatomical structure**			**Coordinates**					
Main Effect	**Region**	**Direction**	**Side**	**x**	**y**	**z**	**Cluster size**	**F-value**	**p-vlaue**
Group								F (1,139)	
	Supramarginal gyurs	C > D	L	-52	-46	34	81	19.02	<0.001 uncor
	Superior temporal sulcus	C > D	R	54	-20	-12	35	19.50	<0.001 uncor
Condition								F (1,139)	
	Superior temporal gyrus	A > AV > V	L	-56	-20	0	2834	169.80	<0.05 FWE-corr
	Middle occiptital cortex	AV > V > A	L	-24	-98	-2	2521	137.00	<0.05 FWE-corr
	Angular gyrus	AV > V > A	L	-48	-68	2	52	21.32	<0.05 FWE-corr
	Superior temporal gyrus	A > AV > V	R	64	-12	-8	3213	238.85	<0.05 FWE-corr
	Inusla	A > V > AV	R	38	22	-4	201	32.71	<0.05 FWE-corr
	Middle occiptital cortex	V > AV > A	R	38	-92	-2	33779	163.99	<0.05 FWE-corr
Stimuli								F (1,139)	
	Inferior frontal operculum	PW > W	L	-52	10	2	123	38.48	<0.05 FWE-corr
	Supplementary motor area	PW > W	L	-2	4	62	36	37.94	<0.05 FWE-corr
Interaction								F(2,139)	
Group x Condition	Insula		R	38	22	-4	129	14.96	<0.001 uncor
Group x Stimuli	Postcentral gyrus		L	-24	-32	44	91	21.22	<0.001 uncor
Condition x Stimuli	Temporal Sup		R	54	-10	-10	47	10.00	<0.001 uncor
	outside parahipp		R	34	8	18	31	9.48	<0.001 uncor

Main Effects

Reduced hemodynamic brain activation for dyslexic individuals compared to non-dyslexic individuals adults, independent of modality and stimuli, were revealed in the middle and superior temporal sulcus (STS) on the right hemisphere ($F_{(1,139)}$=19.5, p<0.001) and the leftward supramarginal gyrus (SMG) ($F_{(1,139)}$=19.02, p<0.001) (see Figure 24). Moreover, significant interactions between group and modality were found in the rightward insula ($F_{(2,139)}$=14.96, p<0.001), as well as between group and stimuli in the left hemispheric postcentral gyrus ($F_{(1,139)}$=21.22, p<0.001) (see Figure 24).

Furthermore, there were main effects for modality with the strongest hemodynamic responses for AV compared to V and A presented stimuli being found in the leftward angular gyrus (AG) ($F_{(1,139)}$=21.32, p<0.005 FWE) and the right middle occipital cortex ($F_{(1,139)}$=137, p<0.005 FWE). The strongest activations for A, compared to AV or V presented stimuli, were elicited in the STG in the right ($F_{(1,139)}$=238.85, p<0.005 FWE) and on the left ($F_{(1,139)}$=169.80, p<0.005 FWE) hemisphere, as well as in the insula ($F_{(1,139)}$=32.71, p<0.005 FWE). Visually (V) presented stimuli were most prominently processed in the right middle occipital cortex ($F_{(1,139)}$=163.99, p<0.005 FWE).

Increased activations for PW, compared to W, were revealed on left hemisphere in the inferior frontal operculum/ rolandic operculum ($F_{(1,139)}$=38.48, p<0.005 FWE), as well as in the supplementary motor area (SMA) ($F_{(1,139)}$=37.94, p<0.005 FWE).

Correlations With Spelling Performance

In order to more elaborate the findings we calculated multiple regressions between performance measures on the standardized spelling test (“Rechtschreibungstest”) and the hemodynamic response for the different modalities and stimuli. All significant clusters ($k \geq 30$) represent significant correlations and are listed in Table 5.

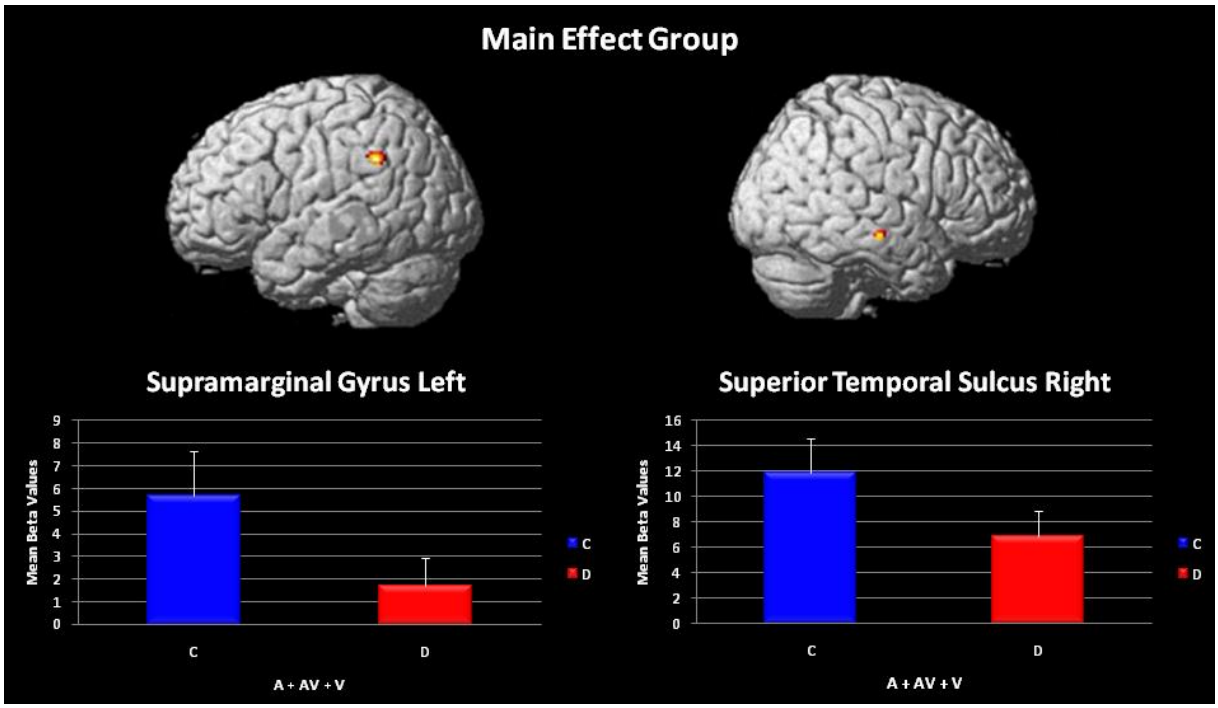

Figure 24 illustrates enhanced neuronal responses for non-dyslexic (C) compared to dyslexic (D) adults in the left hemispheric SMG and rightward STS.

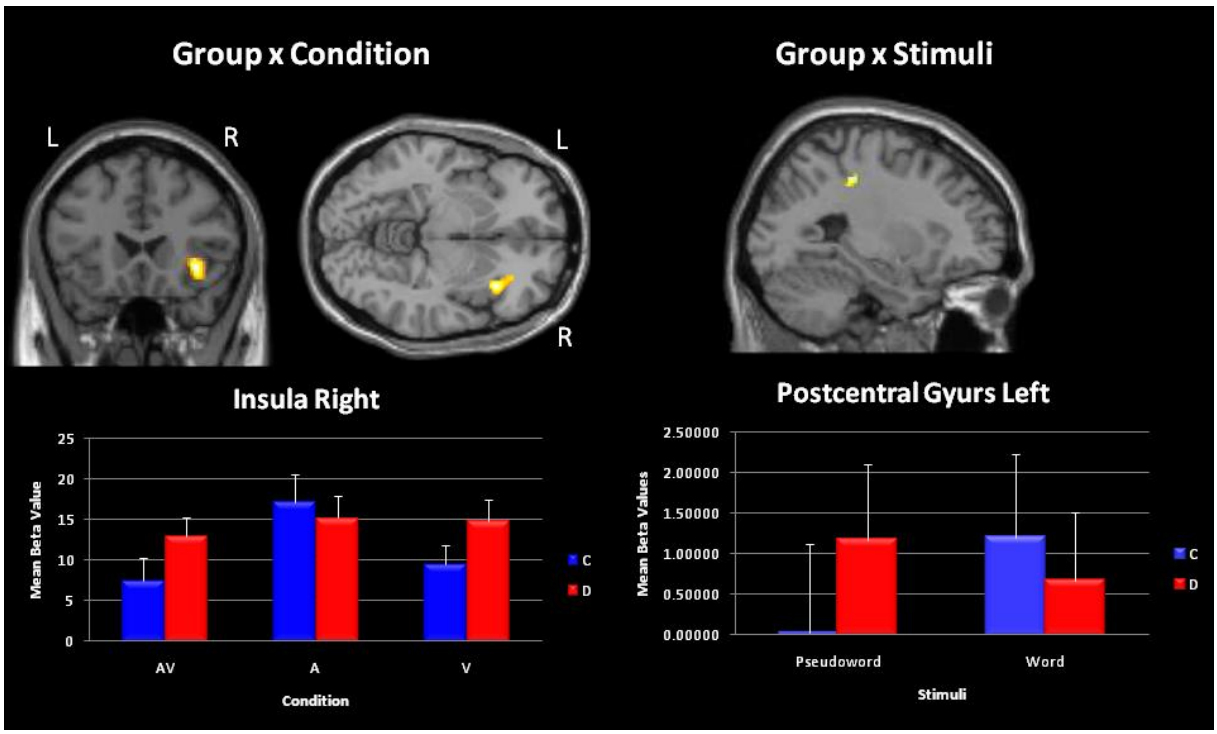

Figure 25 shows a significant interaction between group and condition in the rightward insula and a significant group by stimuli interaction in the postcentral gryus on the left hemisphere.

.

Table 5: Correlations of activation peaks and spelling performance

Direction	Condition	Location	Side	x	y	z	Cluster size	T(23)	p-vlaue
positive	AV PW	SMG	L	-54	-42	34	75	5.08	<0.001 uncor
		Middle Occipital	L	-36	-76	34	129	4.93	<0.001 uncor
		Precuneus	R	12	-62	38	155	4.99	<0.001 uncor
		Middle Occipital	R	34	-78	36	42	4.46	<0.001 uncor
negative	AV PW	Calcarine	L	-14	-48	6	39	4.38	<0.001 uncor
positive	A PW	Sup med	L	-12	28	38	43	4.17	<0.001 uncor
		Middle temporal gyrus	R	40	-54	4	58	4.55	<0.001 uncor
		Insula	R	40	18	-14	33	3.99	<0.001 uncor
positive	A W	Precuneus	L	-14	-68	54	49	4.07	<0.001 uncor
		Occipital Mid	L	-22	-82	12	37	3.84	<0.001 uncor
		Anterior intrapareital sulcus	R	34	-38	36	121	5.62	<0.001 uncor
		Frontal Mid	R	50	42	6	56	4.32	<0.001 uncor
		Insula	R	40	18	-12	42	4.21	<0.001 uncor
		Precuneus	R	12	-72	42	84	4.14	<0.001 uncor
positive	V PW	Lingual gyrus	L	-22	-82	2	69	4.90	<0.001 uncor
		Occipital Mid	L	-40	-72	30	95	4.49	<0.001 uncor
		Frontal Mid	L	-22	22	52	53	4.47	<0.001 uncor
		Temporal Mid	R	48	-20	-8	36	4.10	<0.001 uncor
negative	V PW	Precentral	L	-36	4	34	62	4.78	<0.001 uncor
		SMA	L	-10	-2	52	169	4.61	<0.001 uncor
		Putamen	L	-22	6	-4	38	4.15	<0.001 uncor
		Frontal Sup	R	20	50	20	123	4.72	<0.001 uncor
positive	V W	Front Sup	L	-16	20	44	54	4.40	<0.001 uncor
negative	V W	Premotor cortex	L	-14	0	60	33	4.04	<0.001 uncor
		Front Sup	L	-18	48	20	46	4.03	<0.001 uncor

Discussion

The present study was designed to examine the hemodynamic responses involved in unimodal (A and V), as well as in bimodal (AV) processing of words and pseudowords in dyslexic and non-dyslexic adults, during their performance of a lexical decision task. This paradigm permits further insight into the neuronal correlates of developmental dyslexia.

Behavioral Data: Performance

By running a pre-experiment outside the scanner, we could confirm that both groups were able to reliably recognize the words and pseudowords within 1 second of stimulus presentation. The behavioral data collected during the fMRI experiment revealed that the accuracy scores obtained by each group, during the lexical task did not differ. This finding indicates that both groups could identify the disyllabic stimuli consisting of five letters to the same degree. Nevertheless, both groups processed words and pseudowords more accurately in the bimodal (AV) condition, compared to the unimodal (V or A) condition: this indicates cross-modal facilitation (Forster, Cavina-Pratesi, Aglioti, & Berlucchi, 2002).

The behavioral data reaction times that were collected during the fMRI experiment did not evidence group differences. We expected to find similar behavioral patterns for reaction times and for accuracy rates. We did not, however, find cross-modal facilitation effects for reaction times; instead, longer reaction times for aurally presented stimuli, as opposed to visually or audiovisually presented stimuli, were observed. One cannot rule out the possibility that ambient scanner noise may have interfered with the auditory presentation of words.

Nevertheless, visually presented stimuli were detected as quickly as audiovisually presented stimuli. This indicates that the processing of stimuli was dominated by the visual system. Additionally, there is evidence that words compared to pseudowords are identified faster in all modalities, such as, aurally, visually and audiovisually. This finding supports the dual route model (Coltheart et al., 1993; Coltheart et al., 2001), which suggests that words are processed by the direct route since they are stored in the orthographical lexicon. In contrast, processing pseudowords involves the requirement of applying phoneme to grapheme rules, which results in the incorporation of the indirect route and hence longer computation time.

fMRI-Data:

Although the behavioral data collected during the fMRI experiment did not reveal any group differences, the hemodynamic responses varied as a function of group in several regions. This

nonexistent group difference may indicate that ceiling effects occurred. Alternatively, individuals with dyslexia might have applied compensatory strategies.

The Dorsal and Ventral Streams of Language Processing

Non-dyslexic, compared to dyslexic individuals, showed enhanced hemodynamic responses in multimodal regions, such as, the right STS (ventral), as well as the left SMG (dorsal). This pattern was generally observed irrespective of modality (A, V or AV) and stimulus attributes (W, PW). The involvement of left dorsal and bilateral ventral streams when processing phonetic cues and performing reading tasks supports previous findings (Hickok et al., 2007; Saur et al., 2008; Zaehle, Geiser, Alter, Jancke, & Meyer, 2008). As early as 1891, Dejerine suggested that the posterior aspect of the superior temporal gyrus (STG), as well as a portion of the posterior parietal brain, such as, the SMG and the AG in the inferior parietal lobe (IPL) are critical for reading (Dejerine, 1891). According to a review on the neuro-anatomy of reading, the ventral pathway plays a key role in connecting the visual association cortex to language regions in the left temporal lobe. Circuits for visual processing are located in the left occipito-temporal cortex regions, and become, through practice, increasingly sensitive to processing printed word. Hence, practice offers the development of a word form system, which enables fluency in word recognition (Brem et al., 2010).Notably, a former meta-analysis suggests that the left dorsal pathway is involved in phonological processing (Bolger, Perfetti, & Schneider, 2005; Henderson, 1986). A PET study, revealed higher blood flow in the posterior part of the left dorsal pathway, namely, the left SMG during phonological pronunciations (Rumsey et al., 1997b). Accordingly, the SMG has been suggested to play an important role in the perception and production of phonemes (Caplan, Gow, & Makris, 1995; Ojemann, Ojemann, Lettich, & Berger, 1989).

The Recruitment of the SMG

The reduced hemodynamic response in dyslexics, compared to non-dyslexics, in the left hemispheric SMG is in line with previous studies that have investigated developmental dyslexia. When processing words, dyslexic adults (Eden et al., 2004; Rumsey et al., 1999) and dyslexic children (Aylward et al., 2003) exhibited reduced activation in the left parietal region. Additionally, when reading sentences, reduced bilateral parietal hemodynamic responses were found in children (Meyler et al., 2008). The magnitude of the hemodynamic response in the left temporoparietal cortex is correlated with the improvement in oral language ability in dyslexic children (Temple et al., 2003).

The leftward temporoparietal region is, in addition to phonological processing, considered to provide cross-modal relation of auditory and visual processes during reading (Gabrieli, 2009). It has been proposed that the posterior parietal region receives multimodal inputs. Furthermore, studies have identified the posterior parietal region as an area involved in a wide range of sensory, motor, and attention functions. Thus, the SMG and AG have generally been considered to serve as mediators: relating the output from orthographic processing in extra striate regions (e.g. the lingual gyrus) to lexical and linguistic representations (Geschwind, 1965).Therefore, these regions play a pivotal role in mapping the visual percept of the grapheme onto the phonologic representation of the language system (Damasio et al., 1983). The main effect of group that we found in this study, indicates that the SMG and AG might be important relay stations processing phonological information from different modalities, irrespective of word class; thus, these regions might integrate audiovisual information. We suggest that this audiovisual integration is essential for phoneme to grapheme mapping and, thus, for decoding written contents.

The involvement of audiovisual processing, reflected by the SMG, is strengthened by the positive correlation between activity in this area when pseudowords are presented audiovisually and spelling performance as is shown by the regression analysis (see Table 5). The positive correlation between activity in the SMG and processing pseudowords, which we found in this study, indicates that the neuronal response in this region is associated with phonological but not semantic processing. This is supported by the notion that pseudowords are decoded by applying grapheme to phoneme correspondence rules. This means that the visual percept of print must be transformed in sound representation of the phoneme.

The Recruitment of STS

The reduced hemodynamic response in dyslexic adults compared to non-dyslexic adults in the STS on the right hemisphere, corroborates the assumption that the right temporal lobe also contributes to language processing (Meyer, Friederici, & von Cramon, 2000; Vigneau et al., 2010). Apparently, the lack of STS activity in dyslexic adults may imply their deficient language skills. Nevertheless, the finding of the group effect does not allow us to draw firm conclusions regarding the extent to which the processing of language comprehension might have been affected. Previous studies demonstrate bilateral activation in the middle posterior STS when processing phonetic and phonological information (Hickok, 2009). A prevailing model suggests that temporal signal attributes are preferentially processed within the left hemisphere whereas spectral features, such as, dynamic pitch and prosody are predominantly processed

within the right hemisphere (Zatorre & Belin, 2001; Zatorre & Gandour, 2008). Hence, the left STS/STG has more likely been considered to play an important role in speech (Ghazanfar et al., 2006; Specht, Osnes, & Hugdahl, 2009) processing, and the right temporal lobe is rather associated with slow acoustic modulations of spoken language (Geiser, Zaehle, Jancke, & Meyer, 2008; Meyer, Alter, Friederici, Lohmann, & von Cramon, 2002). The occurence of right STG/STS activation is particularly derived from experiments that use passive tasks, as well as lower-level auditory control stimuli, and has predominately been associated with acoustic analysis (Turkeltaub & Coslett, 2010). Nevertheless, both hemispheres, including the left and right non-primary auditory cortices, might participate in one critical intermediate computation: the analysis of the auditory signal on multiple timescales (Boemio, Fromm, Braun, & Poeppel, 2005; Poeppel, 2003). Although there are important computational differences assumed between the left and right hemisphere, the processing reflects a continuum, rather than an absolute functional difference between the two hemispheres (Hickok et al., 2007).

Additionally, the STS has been implicated to contain multimodal areas that receive visual, somatosensory, auditory projections in monkeys (Seltzer et al., 1994), as well as in humans (Beauchamp, Argall, Bodurka, Duyn, & Martin, 2004). The STS has been considered to integrate audiovisually presented speech and non-speech stimuli (Beauchamp, 2005; Calvert, Campbell, & Brammer, 2000; Miller & D'Esposito, 2005; Sekiyama, Kanno, Miura, & Sugita, 2003). Evidently, the posterior STS has been associated with audiovisual integration (Hein & Knight, 2008), input buffering of speech, and interaction with motor systems for speech (Ackermann & Riecker, 2004; Turkeltaub et al., 2010).

As regards dyslexia, our data coincide with previous studies that elucidate the audiovisual integration of congruent and incongruent grapheme to phoneme conversion in dyslexic adults (Blau et al., 2009) and dyslexic children (Blau et al., 2010). Dyslexic readers failed to modulate the response to speech sounds when those sounds were presented together with both congruent and incongruent visual letters in the bilateral STS. The authors interpreted these findings as an impaired integration mechanism of letter-speech-sounds in dyslexic adults that is partly accommodated by the STS (Blau et al., 2009). Additionally, these authors observed that the dyslexic compared to non-dyslexic adults displayed considerably reduced STG responses to auditory stimulation. The reduced neuronal responses of dyslexic adults in a multisensory region may speak in favor of the view that the audiovisual integration of phoneme to graphemes, which is essential for word and pseudoword decoding, might be a core problem in dyslexic individuals.

The Involvement of the Insula

Significant hemodynamic interaction between groups by modality emerged within the insula in the right hemisphere. Dyslexic compared to non-dyslexic adults showed reduced hemodynamic responses to only aurally and increased responses to only visually as well as audiovisually presented stimuli. Our data indicates that the insula plays a pivotal role in both unimodal (V and A), as well as bimodal (AV) processing of linguistic stimuli (see Table 4, Figure 25). The insular cortex is involved in a wide variety of functions ranging from motor control, language, music, vocalization, multimodal integration, homeostatic regulation, emotion to pain (see for a review Mutschler et al., 2009). Whereas the posterior part of the insula is associated with motor aspects of spoken language (Ackermann & Riecker, 2010), the anterior insula is activated across multiple sensory, as well as cognitive domains (Menon & Uddin, 2010). In particular, the anterior-dorsal part of the insula has been identified as relevant for the encoding of auditory information (Kötter, 2008), such as, processing language and music, as well as perception of vocalization (Mutschler et al., 2009).

Additionally, the insula has been considered as an intermediate site between a primary sensory area and a high-order association area that integrates auditory information with other associative functions (Bushara, Grafman, & Hallett, 2001; Lewis, Beauchamp, & DeYoe, 2000). Imparticular, the right hemispheric insula is suggested to be a multimodal integration area that responds to visual, tactile, and auditory stimuli (anterior > posterior); activation, however, was less prominent than in other multimodal areas such as the right temporoparietal junction (Bamiou et al., 2003).

According to our results (see Table 4), pure auditory stimuli evoked the strongest hemodynamic response in the right anterior insula, followed by the visual and audiovisual stimuli. Previous reports concur our findings that the right insula participates in several auditory processes that include: various aspects of auditory temporal processing (Bushara et al., 2001), sequencing sounds, musical rhythm processing, detection of moving sounds (Lewis et al., 2000), and speech melody (Meyer, Alter, & Friederici, 2003).

In addition, the regression analysis (see Table 5) yielded a positive correlation between hemodynamic response in the rightward insula and spelling skills, which is due to the aurally presented words and pseudowords. This finding indicates that deficient spelling, which occurs in developmental dyslexia, is associated with a response reduction in the right anterior insula to auditory stimulation of word-like stimuli. Our results demonstrate that dyslexic individuals, compared to non-dyslexic individuals, showed a reduced response for the aurally presented stimuli and enhanced activity in the visual and audiovisual mode in the right anterior insula.

These findings coincide with previous studies that observed atypical responses in the anterior insula due to speech stimuli in dyslexic individuals (Steinbrink, Ackermann, Lachmann, & Riecker, 2009). The authors of this study argue that this reduced response reflects a deficient temporal processing in developmental dyslexia. Impairments in temporal processing of short lasting stimuli have been suggested to cause the phonological processing deficit in dyslexics (Temple, 2002). Alternatively, the phonological deficit theory posits that the phonological processing deficit is manifested in a reduced phonological awareness. A study investigating the phonological awareness in young beginning readers revealed an association between increased neuronal responses in the left inferior frontal gyrus and insula and better reading skills (Bach et al., 2010). Another study, which employed a rhyming task that required phonological awareness, also demonstrated no activation of the left insula in dyslexics compared to non-dyslexics (Paulesu et al., 1996). Finally, it has been concluded that insular dysfunctions, as seen in dyslexics, might cause disconnections between the anterior and posterior speech areas, which in turn results in defective phonological processing (Paulesu et al., 1996). A sub-function of phonological processing, namely, phonological retrieval involves integration of activity in the anterior insula/frontal operculum with posterior superior temporal sulci of the left posterior inferior temporal cortex (Bamiou et al., 2003).

The visual stimulus presentation resulted in enhanced hemodynamic responses for dyslexic compared to non-dyslexic adults; this supports previous findings. Visually presented letters, words and pseudowords, or explicit reading of visually presented words and pseudowords elicited enhanced neuronal activity in the right insula in dyslexics, compared to non-dyslexics (Maisog, Einbinder, Flowers, Turkeltaub, & Eden, 2008).

In sum, the group by modality interaction in the right insula may reflect impairment in the integration of aurally presented phonological information with associative functions in the visual domain. Thus, we suggest that amongst others it is this deficient integration mechanism of visually and aurally presented information, which causes the phonological processing impairments associated with developmental dyslexia.

Phonological Processing in the Postcentral Gyrus

We observed left postcentral gyrus involvement provided by a significant group by stimuli interaction. Due to this analyses dyslexics elicited enhanced neuronal responses to pseudowords and non-dyslexic adults showed increased activity for words. Anatomical labeling, using the Harvard-Oxford Subcortical Structural Atlas, indicates that this finding should be interpreted cautiously. Despite of the fact that previous studies demonstrated the involvement of

the postcentral gyrus during processing words and pseudowords (Rumsey et al., 1997b). Accordingly, this recruitment has been associated with phonological processing (Nadeau, 1988; Rumsey et al., 1997b; Tabuchi, Fujii, Suzuki, Endou, & Yamadori, 2000). Along this line Rumsey and colleagues (1997) observed that non-impaired adult readers showed bilateral activation in the perirolandic cortex (pre-/postcentral gyri) during a phonological and lexical decision task that used words and pseudowords. The bilateral activation in the postcentral gyri in response to the lexical decision task is replicated by other studies. In addition, this region has been involved when reading aloud (Carreiras, Mechelli, Estevez, & Price, 2007); therefore, it has been suggested that the activation in this region is associated with lexical decision tasks and by hearing the sound of speech when reading aloud (Carreiras et al., 2007).
A meta-analysis pertaining to research conducted with dyslexic individuals, revealed decreased activations in the right pre/postcentral gyrus (Maisog et al., 2008). Nevertheless, non-phonological treatment (virtual reality in a three-dimensional computer environment) during auditory-repeat/auditory-match contrast increased and normalized activation in the left postcentral gyrus in dyslexic children. This might be a result of the virtual reality treatment, which may have improved the magnocellular function. In addition, decreased and normalized activation in the left postcentral gyrus in dyslexic children has also taken place after phonological treatment (Richards et al., 2007). Due to the fact that pseudoword reading does not have access to automatic routines it is more phonologically demanding; consequently, it is particularly challenging for dyslexic individuals. Dyslexic individuals cannot rely on semantic cues when analyzing phonemes in spoken words or mapping letters onto phonemes; they need to recruit more attentional resources, in order to perform pseudoword decoding tasks. Therefore, we posit that dyslexic individuals recruit greater neuronal circuits when decoding pseudowords.

Conclusion

The present study investigated the neural mechanisms in dyslexic and non-dyslexic adults performing a lexical decision task, which involved stimuli that were presented either unimodally (A or V) or bimodally (AV). This study is based on the foundation that word decoding is a bimodal task which requires that the orthographic representation (grapheme) has to be transformed to the phonological representation (phoneme). Our current data evidence decreased neuronal responses in associative areas, namely, the left hemispheric SMG and rightward STS in dyslexic compared to non-dyslexic adults, which occurred irrespective of presented modali-

ty or lexical content. This notion is supported by the involvement of the insula, a region that has been considered as a multimodal integration area (Bamiou et al., 2003). Hence, our data index atypical responses in multimodal convergence zones. This indicates that dyslexic, compared to non-dyslexic adults recruit neuronal circuits that mediates processing audiovisually presented phonological information in a less proficient way. It is possible that impairments in one unisensory modality even influence the other modality. Accordingly, the neuronal interaction of these unisensory areas may cause abnormal responses in the multisensory regions. We therefore suggest that these atypical responses reflect deficient phoneme to grapheme mapping associated with developmental dyslexia.

Finally, the faster reaction times in response to words, rather than pseudowords, support the dual route theory. This theory claims that words are processed by the direct pathway and pseudowords by the indirect pathway. Computations recruiting the later pathway are assumed to be more time demanding.

Acknowledgment

This project was supported by the Research Funding University of Zurich (56234102) and (56234103) as well as SNF-grant nr. 320000 – 120661.

8.4 Experiment IV: Computer Based Learning of Spelling Skills in Children With and Without Dyslexia

Monika Kast*[1], Gian-Marco Baschera*[2], Markus Gross[2], Lutz Jäncke[1] & Martin Meyer[1]

[1]Department of Neuropsychology, University of Zurich, Switzerland
[2]Institute for Computational Science, ETH Zurich, Switzerland
*The first and second authors contribute equally to this work

Submitted in Annals of Dyslexia

Abstract

The spelling training software examined in a previous study (Kast, Meyer, Vogeli, Gross, & Jancke, 2007) recodes words into multi-sensory representations comprising visual and auditory codes. These original codes represented letter and syllable based information. For the present study we expanded the nonverbal information with a phonological cue and enhanced the word selection controller by a phoneme-based student model, which allows for an adaptation to individual spelling difficulties.

In our first analysis we compared the learning progress of children with dyslexia working with the previous software (n=28), as well as our adapted software version (n=37). Moreover, we investigated the spelling behavior of children with dyslexia (n=37) and matched children without dyslexia (n=25). To gain deeper insight into which factors are relevant for acquiring spelling skills, we analyzed the influence of cognitive abilities, such as, attention functions and verbal memory skills, on the learning behavior. All investigations of the learning process are based on learning curve analyses of the collected log-file data.

The results evidence that children with dyslexia benefit significantly from the additional phonological cue and the corresponding phoneme-based student model. Actually, children with dyslexia improve their spelling skills to the same extent as children without dyslexia, and were able to memorize phoneme to grapheme correspondence when given the correct support and adequate training. In addition, children with low attention functions benefit from the structured learning environment. Generally our data showed that memory sources are supportive cognitive functions for acquiring spelling skills and for using the information cues of a multimodal learning environment.

Introduction

The Phonological Deficit in Developmental Dyslexia

Spelling and reading skills are essential in modern societies where information is commonly provided by written media. In the case of developmental dyslexia (DD) the acquisition of these cultural techniques is impaired. Individuals affected by DD are characterized by low spelling and writing skills in spite of having an average IQ, good educational support and a solid social background (World Health Organization, 1993). Thus, DD is a learning disability with a specific language-based disorder of constitutional origins. The difficulties are manifested in reading difficulties and as a conspicuous problem with acquiring proficiency in writing and spelling (Lyon, Shaywitz, & Shaywitz, 2003).

The causes of spelling and reading failure are still debated. There are several theories focusing on the various impairments suffered by individuals with dyslexia, namely, general auditory (Baldeweg, Richardson, Watkins, Foale, & Gruzelier, 1999; Farmer et al., 1995; Reed, 1989; Tallal, 1980), visual (Livingstone et al., 1988; Lovegrove et al., 1980; Stein et al., 1997) or motor impairments (Nicolson et al., 1990; Rudel, 1985; Wolff et al., 1990). The most accepted theory is the phonological processing deficit hypothesis (Bradley et al., 1983; Ramus et al., 2003c). This theory claims poor phonological awareness that manifests as an impairment in the phoneme to grapheme conversion (Frith, 1985).

Early readers have to learn to pair printed letters of the alphabet, which are represented as visual symbols, with phonemes, which are represented verbally (Adams, 1990; Snowling, Bishop, & Stothard, 2000a). The acquisition of this culturally defined letter-sound knowledge is a critical and fundamental skill for learning to read and spell (Byrne, 1998; Muter et al., 2004). Extended practice of symbol-sound learning leads to improved word recognition (Li et al., 2009). Thus, reading skills have been linked with paired associative learning, i.e. the ability to associate a verbal and visual stimulus with each other (Hulme et al., 2007).

In literate adults, the phoneme to grapheme mapping occurs rapidly and automatically (Paulesu et al., 1996) and can be considered an over-learned paired association process (van Atteveldt et al., 2007b). However, individuals with dyslexia often have extreme difficulties in learning the letter-sound correspondence and a high level of these culturally defined associations may never be reached (Vellutino et al., 2004). Additionally, individuals with dyslexia show difficulties in learning the association between an abstract form and nonsense syllables (Gascon & Goodglass, 1970; Vellutino, Steger, Harding, & Phillips, 1975). On the contrary, individuals with dyslexia performed normally on nonverbal paired association tasks such as

learning to associate one abstract shape with another (Goyen & Lyle, 1971; Vellutino et al., 1975). These problems in visual-verbal association tasks and the lack thereof in visual-visual mapping tasks were found in both Chinese and Western children with dyslexia (Li et al., 2009; Messbauer & de Jong, 2003). Messbauer and de Jong (2003) argued that the difficulty with visual-verbal association tasks, involving words and nonwords, did not reflect problems in the acquisition of new phonological representations but was instead more likely to represent a general phonological learning difficulty.

The aforementioned phonological learning difficulties are linked with a reduced phonics-based memory as exhibited by individuals with dyslexia. Therefore, reduced working memory may cause problems in maintaining phonological information in a particular sequence (Goswami, 2005). It has been suggested that children with dyslexia compared to children without dyslexia use different memory strategies. While children with dyslexia rely on a nonphonological, visual coding strategy for the mediation of the written words in working memory, children without dyslexia use phonological coding (Miller & Kupfermann, 2009).

Multisensory Learning

Studies pertaining to learning, as well as investigations of memory have predominantly focused on learning stimuli consisting of a single sensory modality or on unisensory memories. In recent years it has been suggested that in natural environments information is mostly integrated across multiple sensory modalities (Shams & Seitz, 2008). Thus, the human brain has evolved to develop, learn, and operate optimally in multisensory environments. There is evidence that multisensory training, as opposed to unisensory training, promotes more effective learning of information. Additionally, it is assumed that multisensory experiences enrich our memories and influence ongoing processes (Shams et al., 2008). Indeed, how the brain codes rich sensory aspects of a memory during the process of retrieval is still a fundamental question.

Neuronal models predict that brain areas active during sensory-induced perceptions are reactivated during the retrieval of such information. Data obtained by a PET and an fMRI study provide evidence that retrieval of visual information, which had previously been paired with auditory stimuli over an extensive training period, activated both visual and auditory brain areas (Nyberg, Habib, McIntosh, & Tulving, 2000; Wheeler, Petersen, & Buckner, 2000). Also, behavioral data indicates that multisensory encoded experiences enhance perception and facilitate the retrieval of memory. This occurs even if the stimuli were only unimodally presented in the retrieval condition. Associations between meaningful auditory information and

visual codes were more accurately responded to in the retrieval session, than only visually learned stimuli (Lehmann & Murray, 2005).

Computer Assistant Learning

The benefits of multisensory learning and the indication that children with dyslexia use a nonphonological, visual coding strategy were integrated in the production of new computer-based training programs. The advantages of computer games are that they have both recreational and didactic goals. Successful educational games are aiming to capture student's interest; thereby, motivating them to acquire knowledge.

A multi-modal training program based on the approach of associative learning was presented by a Finnish group. They were able to show that reading improved strongly after an association learning of abstract audio-visual material. Their computer-based training of basal components of reading and writing incorporates nonverbal tasks that require audio-visual matching of rhythm, pitch, and intensity. As a result, the trainee's multi-modal coding of speech stimuli improves, which consequently enhances reading and writing capabilities (Kujala et al., 2001). The software examined in the present study is similarly built on the concept of associative learning; however, our visual and auditory stimuli contain additional information about accurate spelling.

Other training programs focus on the core phonological processing deficit. Ecalle and colleagues (2009) present a learning software package that includes audio-visual phoneme discrimination tasks. In their training tasks, orthographic units have to be discriminated based on simultaneously presented phonological units. This helps to improve both reading and spelling skills in children with dyslexia (Ecalle, Magnan, Bouchafa, & Gombert, 2009). The enhanced software examined in the present study visualizes this association between phoneme and grapheme by means of an additional textural code (see section: The spelling software Dybuster).

A third category of training software directly addresses the correct spelling of words. A multimedia program was developed for children, in order to help them build up a relatively stable phonologically underpinned orthographic representation, particularly for learning words with irregular phoneme-grapheme correspondence in Dutch. The findings of this study indicate that practice with spelling pronunciations is as beneficial as practice with visual preview, and it is significantly more effective than practice with normal pronunciation (Hilte & Reitsma, 2006). The strong effect of the visual preview highlights the need for a prevention of misspelled words, as implemented in the software examined in the present study.

To increase the training efficacy of a spelling training, Bodén and Bodén (2007) proposed an evolutionary approach for adapting spelling exercises to suit individual student needs. Similar words are selected if an error has been committed by the user; however, the similarity measure does not consider the error type or position (Bodén & Bodén, 2007). The phoneme-based mal-rules, which have been added to our spelling software, function to represent errors; thereby, permitting a more detailed adaptation to the student's skill set.

The Spelling Software Dybuster

The computer-based German spelling program examined in this study, namely, Dybuster, is based on the concepts of information theory and multi-modal learning (Gross & Voegeli, 2007). The central idea of the training software involves recoding a sequential input string into a multimodal representation by using a set of codes. The program relies on meaningful visual and auditory stimuli, to support the spelling learning process. Previous findings of behavioral data indicate that meaning (e.g. environmental sounds compared to sine wave tones) is necessary to facilitate the retrieval of multisensory encoded information (Lehmann et al., 2005). The visual cues implemented in the learning software use colors and shapes that reflect information about individual letters. Additionally, a topological code in the software that syllabifies the word is implemented. The purpose of the topological code is to provide a clear structure. It supports the children in their serial behavior during spelling because it assists them with putting the letters in the right position. This is in line with the theoretical framework determining the cognitive architecture of spelling (Lashley, 1951). This theory relies on the notion that spelling is an endogenous generation of serial behavior. Therefore, letters are produced one at a time and must be produced in the correct order. The auditory code, which redundantly represents syllable and color information in rhythm and pitch respectively, completes the multi-modal set of codes illustrated in Figure 26. The entire recoding can be applied to other alphabetic languages (Gross et al., 2007).

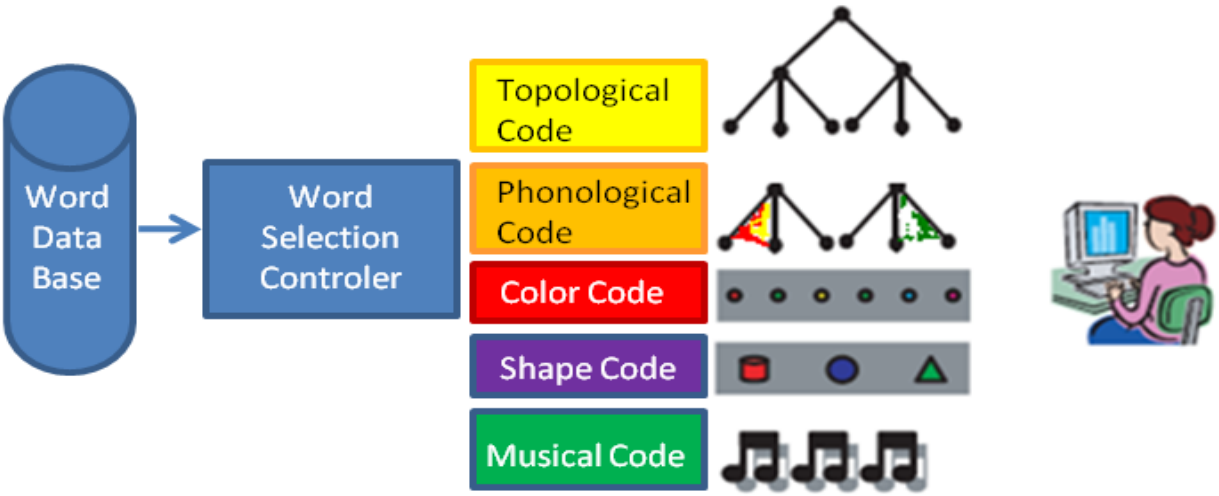

Figure 26: Theoretical framework and conceptual components of the learning software's methods: The word selection controller was adapted for the second user study. The visual and auditory codes of the original software version represented letter and syllable information in color, shape, topological, and auditory cues. The information mediated by the visual system corresponds with the auditory information, i.e. color corresponds with tone and shape with instrument. For the second study, these cues where expanded with a textural code containing phonological information.

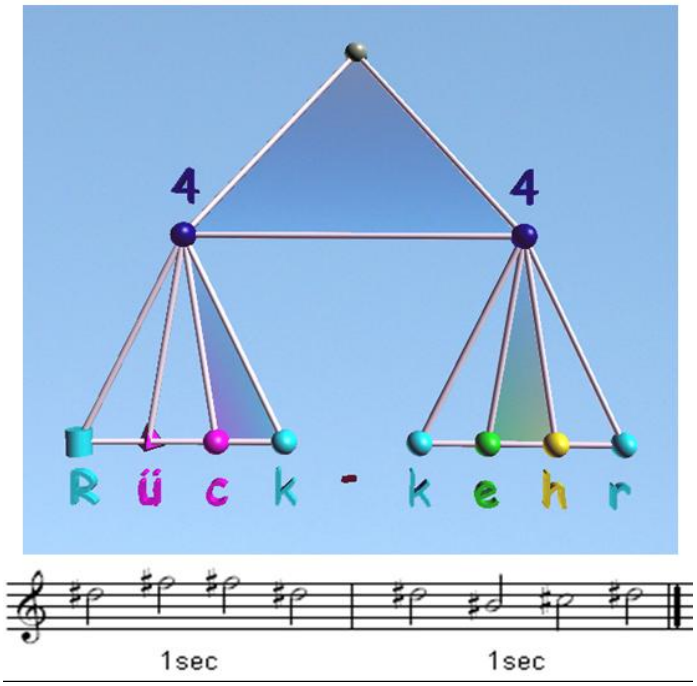

Figure 27: Illustration of the appearance of the components and framework on the screen. The two syllabic word 'Rückkehr' is visualized in the syllabic segmentation. Each syllable lasts one second and the duration of sounds is dependent on the number of letters belonging to one syllable. The correspondence of the graphemes 'ck' and 'eh' to the phonemes /k/ and /e:/ respectively is visualized by the textured triangles between the letters.

The software used in the present study is structured into three different games. In the first game, that is, the color game, students have to learn the association between a letter and a color. Based on the information theoretical model of the spelling program, eight different colors are used. The mapping of letters to colors is the result of a multi-objective optimization,

taking into account that, e.g., letters easily confused by dyslexics, such as *'t'* and *'d'*, map to different colors. In the second game, namely, the graph game, the students are required to segment a word into its syllables and letters graphically. The structure of the word is visualized in a so-called syllable graph. This game provides an important training of segmenting words in syllables; this is a necessary component since there is evidence that the accurate perception of metrical structure in speech and music is critical for phonological development and consequently for the development of literacy (Huss, Verney, Fosker, Mead, & Goswami, 2010).

In the third game, the actual spelling game, the computer-program presents all alternative representations of a word before the students enter the word themselves by using the keyboard. The game proceeds as follows: a graph appears on screen, and the colors and shapes (spheres for small letters, cylinders for capital letters, and pyramids for umlauts) are displayed for all letters, as shown in Figure 27. Then a female voice dictates a word, and the students hear the corresponding melody. While the student enters the word, the computer-based spelling program gives visual and auditory feedback in response to the spelling behavior. This leads to an instantaneous correction of committed errors and prevents the presentation of the erroneously spelled words. This visualization exclusively aids subjects with memorizing the correct word form.

The efficiency of our computer-based spelling program has been demonstrated in a previous study (Kast et al., 2007). In the present study, we aimed to improve the program's effectiveness by adapting the learning program. Therefore, we expanded the framework of the learning software by employing two phoneme-based adjustments, which are based on the theory of phonological processing deficit. According to this theory, DD is manifested in reduced phonological awareness, which in turn leads to difficulties with learning the phoneme to grapheme conversion.

The first adaption to our version was the implementation of an additional textural code. This textural code visualizes the catenation of multiple letters to one grapheme that represents the corresponding phoneme (e.g. 'sch', 'ch', 'ie', 'ei', etc.). As can be seen in Figure 27, the correspondence of the graphemes 'ck' and 'eh' to the phonemes /k/ and /e:/ respectively is visualized by the textured triangles between the letters. This additional code supports the awareness of the phonological structure of the word.

The second adaption was the adjustment of the word selection controller. A novel phoneme-based student model (Baschera & Gross, 2009) was implemented, in order to represent the specific spelling difficulties of individual children. In addition to the already used letter-based

representation, which is able to handle typing errors and letter confusions, the student model incorporates phoneme-based mal-rules, such as, phoneme-grapheme matching (PGM) errors and auditory confusions. This student knowledge representation is continuously re-estimated, based on the error behavior of the present input data. Based on this information, the controller is able to adapt to the strengths and weaknesses of individual children. This enables the controller to expose each child to his or her own specific spelling problems.

Aim of the Study

In a previous study, we investigated the learning progress by means of pre and post spelling tests and demonstrated that both children with and without dyslexia benefit from a three month training course with this computer-based program (Kast et al., 2007). In the current study, we analyzed the learning progress based on the collected log-file data. The phoneme-based student model provides a classification of committed errors and enables analyses based on specific error types, such as, phoneme-grapheme matching (PGM) errors or typing errors. The major part of the investigation focused on spelling learning curves of PGM errors, which reflect the strength of phoneme to grapheme associations.

First, we compared the log file data from the first and the second study. This allowed for an evaluation of the adapted controller and the new phonological cue implemented in the learning software. We expected children with dyslexia who worked with the revised software version to improve their spelling behavior significantly faster than individuals with dyslexia who worked with the original version.

Second, based on data collected in our second study, we investigated the influence of different cognitive factors on the learning progress. These factors included: the indication of dyslexia, memory performances, and attention functions. Comparing children with and without dyslexia allowed us to explore whether both groups would benefit to the same extent from the training or if children with dyslexia, irrespective of the method used, would generally experience more problems acquiring spelling knowledge. Our group decided to evaluate memory functions because it has been suggested that reading problems are associated with impaired memory functions (Schulte-Korne et al., 2004b), which in turn cause reduced phonological representations. Attention functions build the general basis for learning as attention processes control all functions of our cognitive system, provided that tasks are not over-learned and automated (Zimmermann, Gondan, & Fimm, 2002). Attention helps people focus on the relevant information (Posner & Presti, 1987); therefore, we aimed to examine the influence of attention functions on the spelling progress acquired in a structured environment.

Methods

Participants

Twenty-eight dyslexic children participated in the first study (10.36 ± 0.87 SD years of age, 18 females and ten males, 24 right-handed and four left-handed). Thirty-seven children with dyslexia (M_{age}=10.89 ± 0.94 SD years of age, ten females and 27 males, 30 right-handed and seven left-handed) and 25 children without dyslexia (M_{age}=10.29 ± 1.0 SD years of age, 12 females and 13 males, 23 right-handed and two left-handed) were recruited for the second study. The ages ranged from 8- to 12-years-old in both studies. Handedness was assessed by the "Hand-Dominanz-Test" (Steingruber, 1971) in the first study and by the (Annett, 1970) questionnaire in the second study. All children were native Swiss-German speakers with an IQ > 85. Children with an IQ below 85 were excluded from the study.

Children were categorized as dyslexic based on previous diagnosis by trained diagnosticians, such as, therapists or school psychologists. In order to further validate the diagnosis, children with dyslexia were categorized as reading and spelling disabled if their scores were below the 10^{th} percentile on the standardized spelling and reading tests. In contrast, the reading and spelling skills of children without dyslexia were not more than one standard deviation below (≥15.9%) the mean. Children without dyslexia were recruited from responses to letters distributed in elementary schools or presentations in school classes where the program was demonstrated. The recruitment of children with dyslexia was conducted primarily with the assistance of therapists or educational psychology services. Notably, children with and without dyslexia attend public schools. All of the children's parents gave their informed consent for participation in the study as per the Declaration of Helsinki. Experimental procedures were approved by the local Ethics Committee (SPUK).

Table 6: Behavioral pre-test data for the dyslexic children in study1.

	With Dyslexia (n=28)			
Measures	**Mean**	**S.D.**	**Min.**	**Max.**
Age (years)	10.36	0.87	8.83	11.75
Grade of school	3.96	0.84	3.00	5.00
IQ[2]	106.04	12.26	87.00	135.00
Verbal IQ[1]	108.04	12.32	85.00	142.00
Performance IQ[1]	102.93	12.52	87.00	125.00
Wordlist reading error (z)[3]	-2.68	2.83	-14.00	0.65
Wordlist reading time (z)[2]	-4.23	5.43	-27.90	2.20
Text reading time (z)[2]	-2.93	3.48	-17.50	4.25
Text reading error (z)[2]	-4.42	5.13	-25.00	0.14
Spelling performance (z) [4]	-1.20	0.67	-2.40	0.10

[2] HAWIK III
[3] ZLT
[4] SLRT or DRT5

Table 7: Behavioral pre-test data for the children with and without dyslexia in study 2.

	With Dyslexia (n=37)				Without Dyslexia (n=25)				Mann-Whitney	
Measures	**Mean**	**S.D.**	**Min.**	**Max.**	**Mean**	**S.D.**	**Min.**	**Max.**	**Z score**	**Probability**
Age (years)	10.89	0.94	8.08	12.58	10.29	1.00	8.50	12.58	0.805	0.535
Grade of school	4.68	0.85	3.00	6.00	4.32	0.90	2.00	6.00	-1.380	0.168
IQ[5]	113.03	10.99	88.00	128.00	117.92	12.31	95.00	140.00	-1.185	0.236
Verbal IQ[1]	114.34	16.07	52.00	136.00	122.80	12.59	98.00	148.00	-1.997	0.046
Performance IQ[1]	105.89	17.81	39.00	144.00	109.64	14.17	88.00	135.00	-0.751	0.453
Wordlist reading error (z)[6]	-1.59	1.27	-2.85	0.99	0.11	1.45	-2.85	2.05	-4.182	<0.001
Wordlist reading time (z)[2]	-1.96	0.99	-2.85	0.30	0.06	1.31	-2.35	2.50	-5.115	<0.001
Text reading time (z)[2]	-1.81	0.99	-2.85	1.17	0.06	0.83	-1.48	1.75	-5.719	<0.001
Text reading error (z)[2]	-1.88	0.99	-2.85	-0.31	-0.17	0.84	-2.85	1.17	-5.330	<0.001
Reading wordsimilar: Pseudowords time (z)[7]	-1.02	0.80	-2.33	1.06	0.23	0.76	-0.99	1.64	-4.909	<0.001
Reading worddisimilar: Pseudowords time (z)[3]	-0.87	0.86	-2.58	1.06	0.29	0.95	-1.75	1.64	-4.240	<0.001
Spelling performance (z)[8]	-1.48	0.56	-2.55	0.40	-0.16	0.68	-1.00	1.30	-6.066	<0.001

[5] HAWIK III
[6] ZLT
[7] SLRT
[8] SLRT or DRT5

Test Battery and Procedure

Before the training took place, an information event was organized for both children and their parents of the first and the second study, in order to distribute detailed instructions about the study design and the concept of the learning software. Notably, the software is designed in a way that children can accomplish the training for themselves and do not need additional help or parental assistance. Detailed information about the handling of the learning software was presented on the first training day.

After providing general study information and before the actual training began, all study participants underwent a series of standard psychological tests (see for results Table 6 & 7). The test battery for the participants in the first and second study differed slightly. In the first study, children performed the classical German spelling tests, "Salzburger-Lese und Rechtschreibtest SLRT" (Landerl et al., 1997) or "Diagnostischer Rechtschreibtest für fünfte Klassen DRT5" (Grund et al., 1995). This enabled us to quantify their spelling skills. There were two different spelling tests applied because the SLRT contains only norms from the first to the fourth grade. Thus, the DRT5 was administered to the fifth graders. Additionally, all children were required to accomplish a standardized reading test, „Zürcher Lesetest ZLT" (Linder et al., 2000), which permitted the quantification of their reading skills. This reading test contained two subtests, namely, reading of wordlists and texts; performance was measured as time used and errors made. A German intelligence test named "HAWIK III" (Tewes et al., 1999) was also administered, in order to assure average or above-average general cognitive skills in all subjects. In the second study, the aforementioned test battery was expanded with a pseudoword reading test from of the ("Salzburger-Lese und Rechtschreibtest SLRT").

To evaluate verbal memory functions, a verbal learning and retentivity test, that is, the "Verbaler Lern- & Merkfähigkeitstest VLMT" (Lux, Helmstaedter, & Elger, 1999) was administered. This test measures learning performance, as well as short- and long-term memory by using word lists that must be repeated five times and recalled after half an hour.

The attention functions were tested by a version of computer based program called KiTAP that is specifically designed to examine children (Zimmermann et al., 2002). This allowed us to test alertness, flexibility, and impulse control. Alertness forms a crucial role in attention intensity; it constitutes processes of the tonic and phaseal arousal (Posner & Rafal, 1987). Flexibility is the aptitude to adapt to a new situation. The disability to realign focus attention causes preservative and stereotypical behavior (Lezak, 1995). Impulse control is the ability to refrain an inadequate reaction and is tested by a Go/No-Go Task (Drewe, 1975). While the KITAP computes the percentile of reaction time as a measure for alertness, the percentile of

errors is used as a measure of flexibility and impulse control. Low scorers performed half a standard deviation below (≤ 30%), and high scorers performed above (≥ 70%) the mean for a given attention or memory function. The spelling tests were accomplished in a classroom setting. Reading, verbal memory, attention, and IQ tests were conducted in an individual test setting.

Children in the two studies performed the computer-based training for a period of 12 weeks. They were asked to practice about five times a week for 20 minutes each (see Table 8 for detailed information about how the training was monitored from the log file data). No significant differences were found between the training times in the first 30 training days. The training generally took place on participants' home computers. Participants were offered the option of undergoing supervised training at our lab once a week. The meeting at our lab enabled us to monitor the data, which included checking children's working behavior and making sure that no technical problems occurred. For monitoring reasons, the parents of children who did not come to our lab once a week were requested to send us the log-file data. During training, the children worked at their own individual pace and were asked to learn up to 1500 words with the level of difficulty corresponding to their elementary grade. The words contained various types of difficulties, which included: doubling of letters, such as, "Fall" (case), "Strasse" (street) and "Mutter" (mother); silent letters, for example, "Theater" (theater), "Zahl" (number) and "Saal" (hall); and diphthongs, such as, "Räuber" (thief), "Feuer" (fire), and "keine" (none), all belonging to the same group of phoneme-grapheme difficulties. Moreover, the words harbored other difficulties, which are caused by the visual similarity of letters ('d'-'b') or by the auditory similarity of phonemes (/n/-/m/).

Table 8: Information about the training frequency (only spelling game) for each group during the first 30 training days. Notably, inputs per session are the number of entered words

Mean over first 30 training days of:		**Training minutes per session**		**Inputs (words) per session**		**Total training minutes**	
		Mean	**S.D.**	**Mean**	**S.D.**	**Mean**	**S.D.**
1st study	With dyslexia	16.3	2.2	54.7	16.1	581.3	99.2
2nd study	With dyslexia	16.1	2.8	51.9	20.0	573.2	144.4
	Without dys.	16.5	1.9	65.3	21.1	574.2	115.9

Learning Curves

The concept of describing practice effects by simple nonlinear functions in a broad range of tasks is presented in Newell and Rosenbloom's "Mechanisms of Skill Acquisition and the Law of Practice" (Newell & Rosenbloom, 1981). It has become a well-established procedure in the psychology of learning to analyze learning behavior based on such learning curves. However there is an ongoing debate regarding which decay function best fits the relation between proficiency and number of practice trials. Based on the findings of Heathcote and colleagues (2000), we decided to rely on an exponential law of practice. This exponential law of practice describes the process of learning by an exponential decay function

$$P_e(t) = a'e^{-bt} + c,$$

where $P_e(t)$ represents the error probability at time t (Heathcote, Brown, & Mewhort, 2000). For our comparison of the different groups, we are interested in the initial error probability ($a = a' + c$: Error probability at time $t = 0$), the learning progress (b: Slope of the learning curve), and the asymptotic error probability (c: Error probability for time $t \to \infty$). For sake of simplification, we performed the variable transformation $a = a' + c$ and obtained the exponential decay function

$$P_e(t) = (a - c)e^{-bt} + c.$$

Statistics

The student model (Baschera et al., 2009) provides information about the amount of error possibilities in a word and describes the category of committed errors. To compare two groups of children on an error category, we compute the number of error possibilities ($W(t,g)$) and the number of committed errors ($C(t,g)$) of this category at day t for each group g. For example, the word "Zahl" (number) contains five PGM error possibilities, such as "Tzahl", "Tsahl", "Zal", "Zaal" or "Zahll". In contrast, typing this word on a German keyboard entails 17 typing error possibilities. The values ($W(t,g)$) and ($C(t,g)$) are collected for the first 30 training days, i.e., we count only the days that the children were working with the training software. To exclude repetition effects from the analysis, we only consider the first prompt of each word. This procedure ensures that we only examine transfer effects from previously learned rules to newly encountered words. By dividing $C(t,g)$ by $W(t,g)$ we get the weighted mean error probability $P_e(t,g)$ of each group for the first 30 days. This expresses the probability that a child of a given group g committed an error, if such a possibility occurred in a prompted word, at day t.

Then we use a weighted nonlinear least squares method, to estimate the parameters of the exponential fit of both datasets. The number of error possibilities ($W(t,g)$) are used as weights for the estimation. To evaluate the significance of the difference between the two regressions, we run a combined estimation. Every parameter p is replaced by a term $p(1+r_p g)$, consisting of an absolute parameter p for the group $g=0$ and a relative parameter r_p, denoting the relative difference of the parameter p for the first ($g=0$) to the second ($g=1$) group. This results in an estimation of the following form:

$$P_e(t,g) = (a(1+r_a g) - c(1+r_c g))e^{-b(1+r_b g)t} + c(1+r_c g)$$

where g equals zero for the first group and equals one for the second group. r_a, r_b and r_c indicate the relative difference between the corresponding parameters of the two groups and their t-tests return a measure for the significance of the difference.

To avoid an over-fitting to the data, we first reduced the above model for each comparison of the two groups. The reduction is performed by means of a backward model selection based on the AIC score (Akaike, 1974). In the results section the removed parameters will be marked by an "R", which indicates that the model without those features represents the data the best. For example, if r_a is mark by "R", the model considering no differences between the two investigated groups fits the data superiorly and the error probability a is equal for both groups. All the regression analyses and model selections were computed with the statistical software R (http://www.r-project.org).

Data Analysis

The data analyses are based on phoneme-grapheme matching errors (PGM). In orthographically nonshallow languages, such as, English and German, phonemes can be represented by different graphemes. Choosing a wrong grapheme representation for a phoneme is denoted as a phoneme-grapheme matching error. The PGM errors reflect difficulties in the phoneme to grapheme mapping process. These are mostly additions or omissions of silent letters or doubling of letters and are a major difficulty for children with dyslexia. PGM errors account for approximately 30% of all committed errors during both studies. Since the different grapheme representations of a phoneme all sound the same, the correct matching has to be learnt by heart or by acquiring rules. Therefore, the progress in the PGM error probability is an appropriate measure for the learning behavior.

In contrast to PGM, typos are randomly occurring errors that are obviously not related to specific spelling difficulties of words. Typos account for approximately 40% of all the committed

errors. Due to the randomness of typos and their independence of general spelling difficulties, we expect less progress over time. A detailed description of the different error categories provided by the student model can be found in (Baschera et al., 2009).

First, we compared the log-file data from the children with dyslexia in the first study to the children with dyslexia in the second study. The learning progress is evaluated by PGM errors, as well as typing errors; thus, enabling us to investigate whether the children could benefit from the phoneme-based enhancements of the spelling training software. Since the possibilities for PGM errors occur less frequently than for typing errors, the estimated errors probabilities of PGM errors (P_e~0.02) are orders of magnitudes higher compared to typing errors (P_e~0.001).

Second, we analyzed only the log-file data collected during the second study. We demonstrate the comparisons of children with and without dyslexia, as well as the comparison of different groups based on attention functions and verbal memory skills. In these analyses we investigated the phoneme-grapheme matching errors (PGM).

Note that we always compare two groups. However, for attention function and memory performance analysis, we classified all children based on their performance in the standardized neuropsychological tests, independent of their indication of dyslexia. To examine confounding effects between cognitive functions and the absence or the presence of the diagnosis of DD, we applied a t-test for independent samples. The outcome of this procedure demonstrated that there are no significant differences in the cognitive functions between the two groups (with vs. without dyslexia) (see Table 9 for details). The number of children with and without dyslexia in each group is presented in the following table.

Table 9: Cognitive function (memory and attention) comparisons for children with and without dyslexia

	With Dyslexia (n=37)		**Without Dys. (n=25)**		**Mann-Whitney**	
	Mean	**S.D.**	**Mean**	**S.D.**	**T**	**p-value**
Alertness	46.47	25.89	54.44	24.19	-1.22	0.23
Flexibility	46.46	32.67	52.62	33.84	-0.72	0.48
Impuls Control	41.15	29.47	49.18	29.45	-0.94	0.35
Learning Performance	46.07	30.86	51.40	30.16	-0.67	0.50
Short-term Memory	55.82	29.81	58.10	28.53	-0.30	0.77
Long-term Memory	59.73	26.47	61.10	25.78	-0.20	0.84

To further investigate how the subtests of the attention and memory functions are related to each other we applied a parametric correlation analysis. The outcome of this procedure

yielded that the subtests of the attention function alertness and flexibility correlated significantly (r=.277, p<0.05) (two tailed). Additionally, this computation evidenced that all subtests of the memory functions correlated significantly with each other, such as learning performance with short-term memory (r=.652, p<0.01), learning performance with long-term memory (r=.595, p<0.01), and short-term memory with long-term memory (r=.761, p<0.01) (two tailed). Notably, the main finding of this analysis yielded that attention functions were orthogonal to memory functions. None of the sub-test belonging to the attention function (alertness, flexibility or impulse control) correlated significantly with any sub-test of the memory skills (learning performance, short-term memory or long-term memory). Since, our DD sample was in addition not confounded with alertness functions or memory skills, we were able to investigate the influence of individual cognitive functions on the acquisition of spelling skills.

The results of the learning curve estimations are illustrated in the Figures and Tables below. If not stated otherwise, the *black* and *red lines* illustrate the fitted learning curves for both groups. The *red* and *black points* show the measured error probabilities at a given day for the two groups. The plotted error bars denote the 95% confidence intervals for the estimated probability measure of the analyzed error category at this day.

In the Tables, the parameters of the first group are given in absolute values. The difference to the second group is displayed by a relative change. “Pr(>|t|)” shows the significance of each parameter. The "initial error probability" (a) describes the probability of errors at the beginning of the study, which corresponds to the axis intercept. Additionally, r_a represents the relative difference between the first and the second group. The “learning progress” (b) demonstrates the slope of the learning curve and depicts the speed at which children improve during training. The relative difference of the slope between groups is named with r_b. "Asymptotic error probability" (c) indicates the limit of the children's training performance and r_c characterizes the relative differences of this factor.

Results

Children With Dyslexia: First vs. Second Study

Figure 28 illustrates the probabilities of the phoneme-grapheme matching errors (PGM), as well as probabilities of the typing errors (typos) for children with dyslexia in the first and second studies. As expected, both groups with dyslexia start with the same error probability (r_a = R) and show no difference in the asymptotic error probability (r_c = R) for PGM errors

(see Table 10). This result indicates that both groups have similar spelling skills at the beginning of the study and will attain the same limit in the training performance.

The main finding of this analysis is that the group who underwent dyslexia training with the new phoneme-enhanced software version benefitted 154% more from the training (b : Pr(>|t|) = 2e-7), than the individuals who experienced dyslexia training with the old spelling program. Table 10 also illustrates that the probability of committing a typo (a = 0.0006), if such a possibility occurs, is significantly less than for PGMs (a = 0.031). The analysis of the typos revealed that both groups commit approximately the same number of typing errors at the beginning (r_a = R) and at the end (r_c = R) of the training. Additionally, the two groups reduced their typos to the same extent (r_b = R). A significant decrease of typos was observed during the training; however, the learning progress on PGM (b = 0.05) as compared to typos (b = 0.011) was substantially higher.

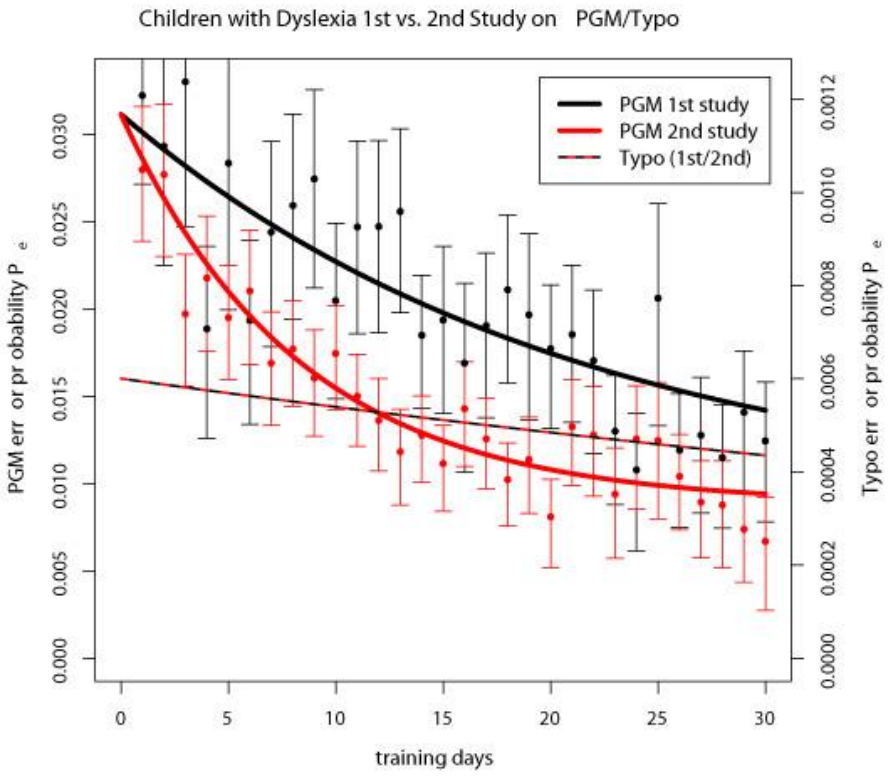

Figure 28: Learning curves of PGM errors (left y-axis) and typos (right y-axis) for the children with dyslexia from the first and second studies. The bold black and red lines illustrate the fitted learning curves for the children with dyslexia from the first study (black) and second study (red). The points and error bars illustrate the PGM error probability estimate for a given day and its 95% confidence intervals. The spelling improvement of individuals with dyslexia from the second study (vs. first study) on PGM was significantly higher; however, in both groups the same typing error behavior was observed.

Table 10: PGM errors and typo results for participants with dyslexia in study 1 and 2. The parameters of the fitted learning curve from the first study are presented in absolute values. The parameters of the second study are displayed as a relative difference compared to first study's parameters.

		Initial error probability		**Learning progress**		**Asymptotic error probability**		
		a	Pr(>|t|)	B	Pr(>|t|)	c	Pr(>|t|)	
		r_a	Pr(>|t|)	r_b	Pr(>|t|)	r_c	Pr(>|t|)	
PGM								
1st study	(abs.)	0.031	2e-16	0.050	7e-09	0.0091	7e-12	0.788
2nd study	(rel.)	R		+154%	2e-07	R		0.907
Typo								
1st study	(abs.)	0.0006	2e-16	0.011	0.0039	R		0.399
2nd study	(rel.)	R		R		R		0.752

Children With vs. Without Dyslexia

Figure 29 presents the learning curves of phoneme-grapheme matching (PGM) errors for children with and without dyslexia, who participated in the second study. As Table 11 depicts, children without dyslexia (as compared to children with dyslexia) showed 21.8% fewer spelling errors at the beginning of the training; they are beginning with a significantly lower initial error probability (r_a : Pr(>|t|) = 5e-08). Our main finding is that both groups were able to significantly improve their spelling proficiency during the training (b : Pr(>|t|) = 3e-08). Importantly, both groups were able to improve their spelling proficiency to the same extent (r_b = R). Furthermore, children without dyslexia as compared to children with dyslexia showed a slightly lower asymptotic error probability (r_c : Pr(>|t|) = 0.04).

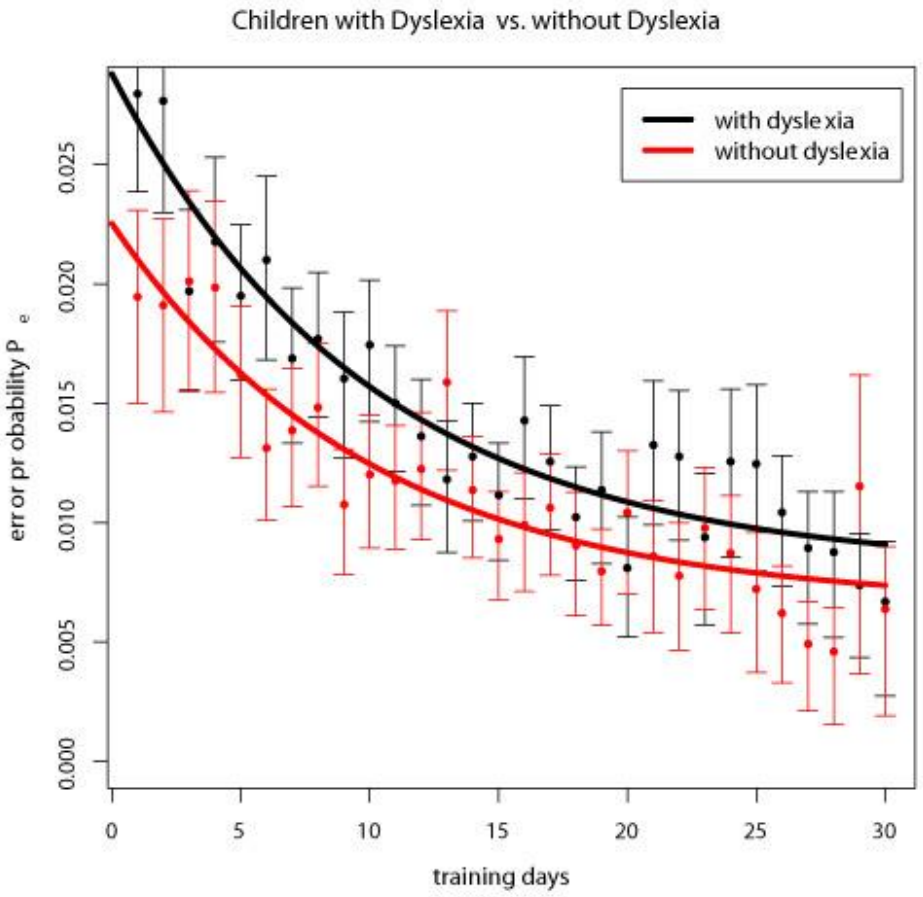

Figure 29: Learning curves for PGM errors of the children with and without dyslexia from the second study. Both groups were able to improve their spelling skills to the same extent.

Table 11: Results of the PGM errors for the children with and without dyslexia

		Initial error probability		**Learning progress**		**Asymptotic error probability**		
		a	Pr(>|t|)	b	Pr(>|t|)	c	Pr(>|t|)	
		r_a	Pr(>|t|)	r_b	Pr(>|t|)	r_c	Pr(>|t|)	
With dys.	(abs.)	0.029	2e-16	0.100	3e-08	0.0080	7e-10	0.908
Without	(rel.)	-21.8%	5e-08	R		-18.3%	0.040	0.818

Attention Functions

In a further step, we analyzed the attention functions influencing the phoneme-grapheme-mapping progress, which involved comparing children with low attention functions to children with high attention functions, based on the data of the second study. As displayed in Table 12, our data showed that children with high compared to low impulse control (r_a = -47.0%, Pr(>|t|) = 1e-14), flexibility (r_a = -46.4%%, Pr(>|t|) = 2e-16), and alertness scores (r_a = -

12.3%, Pr(>|t|) = 0.0038) committed significantly fewer spelling errors at the beginning of the training. Notably, children with low attention functions (i.e. impulse control (r_b = R), flexibility (r_b = R), and alertness (r_b = R)) were able to benefit from the training to the same degree as the corresponding high attention score group. Additionally, the two groups did not differ in their asymptotic error probability in all attention functions (r_c = R). Therefore, it can be expected that children with high vs. low attention functions will attain the same spelling level. Figure 30 illustrates the learning curves for the comparison of the groups with high and low impulse control.

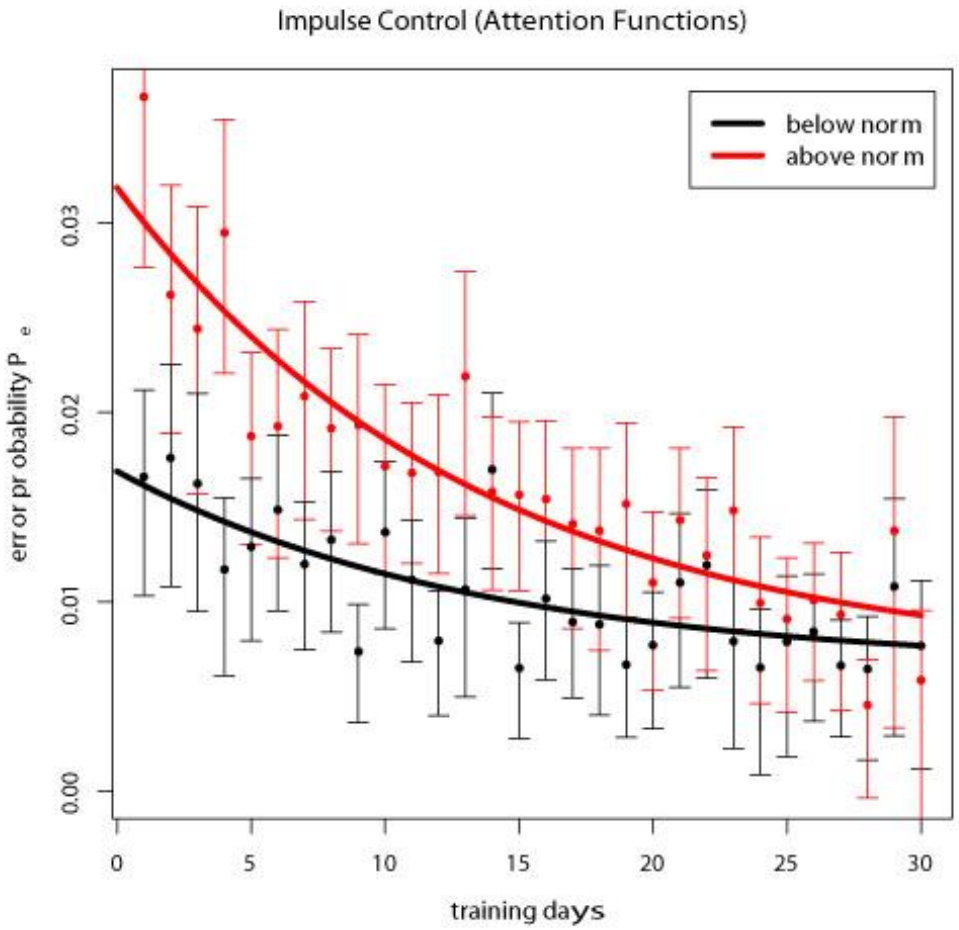

Figure 30: Learning curves for children with high and low impulse control scores on PGM errors. Low vs. high scorers can benefit similarly from the structured environment and the implemented audiovisual codes of the learning software**.**

Table 12: Results of attention functions influence on PGM progress

		Initial error probability		Learning progress		Asymptotic error probability		
		a	Pr(>|t|)	b	Pr(>|t|)	c	Pr(>|t|)	
		r_a	Pr(>|t|)	r_b	Pr(>|t|)	r_c	Pr(>|t|)	
Impulse Control		(below: 11 with dys. / 4 without dys. – above: 6 with dys. / 6 without dys.)						
Below N	(abs.)	0.032	2e-16	0.074	2e-06	0.0066	2e-05	0.815
Above N	(rel.)	-47.0%	1e-14	R		R		0.464
Flexibility		(below: 14 with dys. / 5 without dys. – above: 13 with dys. / 8 without dys.)						
Below N	(abs.)	0.042	2e-16	0.127	5e-11	0.0085	3-16	0.848
Above N	(rel.)	-46.4%	2e-16	R		R		0.837
Alertness		(below: 11 with dys. / 5 without dys. – above: 7 with dys. / 8 without dys.)						
Below N	(abs.)	0.028	2e-16	0.044	2e-16	R		0.754
Above N	(rel.)	-12.3%	0.0038	R		R		0.798

Memory Skills

Children with high vs. low learning performance, short-term memory, as well as long-term memory scores all started at the same level (see for details Table 13); however, compared to low scorers, children with high scores in learning performance (r_b = +126%, Pr(>|t|) = 0.0016), short-term memory functions (r_b = +175%, Pr(>|t|) = 0.0015), and long-term memory functions (r_b = +226%, Pr(>|t|) = 8e-05) exhibited significantly decreased spelling errors during the training. Conversely, the asymptotic error probability did not differ significantly between groups. Figure 31 displays the difference between high and low learning performance.

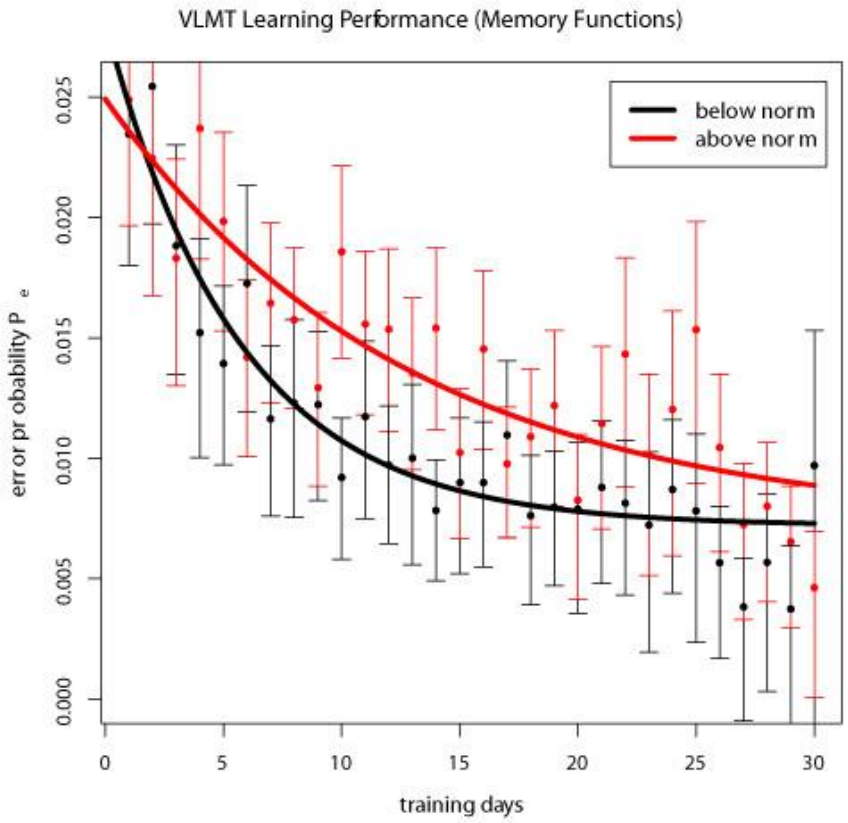

Figure 31: Learning curves for children with high and low verbal learning performance (VLMT) on PGM errors. Children with high, compared to low memory skills, significantly reduced their error probability.

Table 13: Results of memory performances influence on PGM progress

		Initial error probability		**Learning progress**		**Asymptotic error probability**		
		a	Pr(>|t|)	b	Pr(>|t|)	c	Pr(>|t|)	
		r_a	Pr(>|t|)	r_b	Pr(>|t|)	r_c	Pr(>|t|)	
Learn. performance		(below: 14 with dys./ 7 without dys. – above: 9 with dys./ 7 without dys.)						
Below N	(abs.)	0.026	2e-16	0.079	2e-8	0.0072	2e-12	0.777
Above N	(rel.)	+12.7%	0.212	+126%	0.0016	R		0.908
Short-term		(below: 10 with dys./ 6 without dys. – above: 12 with dys./ 10 without dys.)						
Below N	(abs.)	0.022	2e-16	0.036	2e-05	0.0051	0.0017	0.602
Above N	(rel.)	+15.9%	0.090	+175%	0.0015	R		0.901
Long-term		(below: 7 with dys./ 5 without dys. – above: 12 with dys./ 9 without dys.)						
Below N	(abs.)	0.025	2e-16	0.039	5e-05	0.0064	3e-06	0.454
Above N	(rel.)	R		+226%	8e-05	R		0.851

Discussion

This study was designed to investigate the learning curves of children who worked with a computer based spelling training system. First, we aimed to evaluate the efficiency of additional phonological based information implemented in the new version. Second, we analyzed spelling and learning behavior of children with and without dyslexia. Third, we investigated the influence of cognitive functions, such as, memory and attention on the learning progress.

Children With Dyslexia: First vs. Second Study

The most interesting finding of the first analysis was that children with dyslexia who worked with the new software version, compared to children with dyslexia who worked with the first software version, significantly increased their learning performance on PGM errors by +154%. The fact that the children with dyslexia in the first and second study show comparable initial and asymptotic error probabilities on PGM underpins the notion that the two groups did not differ from each other a-priori. This result evidences that the phoneme-based enhancements, such as, textural code and adjusted controller supported the children with their learning behavior.

The additional textural code is implemented based on the notion that the core problem of DD is a phonological processing deficit. This deficit becomes manifest in reduced phoneme to grapheme mapping skills (Byrne, 1998; Ramus et al., 2003c). The additional textural code provides supplementary information to the topological code. Whereas the topological code syllabifies the word, the textural code supplies easily extractable information about the phonological word structure (see textural code on Figure 26 and Figure 27). This results in a segmentation of the word in phonemes and supports the association with their graphemes. The visualization of the association between phonemes and graphemes strengthens the phonological awareness similarly to the audio-visual phoneme discrimination task used in the software that has been evaluated by (Ecalle et al., 2009).

We believe that another important factor responsible for the enhancement of the spelling skills was the phoneme-based word selection controller. This controller identifies the children's individual difficulties based on their error behavior and prompts words containing these problems. In contrast to Bodén and Bodén's (2007) evolutionary approach to word selection, which lacks an error localization or classification, and to the old word selection method of Dybuster, which relies on a letter-based analysis of errors, the new controller accounts for spelling difficulties on a phonological level. For example, if a child struggles with spelling the

word “Zahl” (number) because it does not know that the word contains a silent “h”, then the controller selects and prompts more words containing silent sounds, such as “sehr” (very) or “ahnen” (guess). Therefore, the child is repeatedly confronted with his/her individual spelling problems. Consequently, the child learns the linguistic spelling rules based on the German language and generalizes them to other words after training.

In a supplementary analysis, we investigated the error behavior on typos. The error probability of randomly occurring typing errors is several orders of magnitudes lower than the PGM error probability. Contrary to the group differences in PGM errors, the error behavior as regards typos did not differ between the first and second group of participants with dyslexia.

Moreover, the analysis of typos indicated that in both groups the children slightly decreased their typing error probability. This slight improvement can be explained by the lack of experience of 8- to 12-year-old children in working at a keyboard. We assume that the children gained knowledge about the key distribution on the keyboard through training, which resulted in a weak reduction of the typing errors probability.

Children With vs. Without Dyslexia

Our data demonstrate that the multi-modal training induced a significant decrease in spelling errors, particularly phoneme-grapheme matching errors, in both children with and without dyslexia. This progress was found for words that were presented for the first time. Therefore, children with dyslexia, as well as children without dyslexia showed that they not only memorized the word-form of the target words (i.e. correct spelling) but that they were able to generalize concepts and adopt rules based on the German language. The most significant effect yielded from this research study was that both children with dyslexia and children without dyslexia exhibited the same learning progress, although children with dyslexia were characterized by a significantly higher initial spelling error probability. These results evidenced that both groups benefited from the training and improved their phoneme-grapheme conversion knowledge.

Learning to read and spell requires memorizing and applying the phoneme-grapheme correspondence forwards or backwards. It has been suggested that learning to read and spell permanently changes the nature of phonological representations in the brain (Goswami et al., 2005) and that these orthographically shaped phonological networks are directly linked to additional visuo-orthographical networks. Finding the same learning curve in both groups indicates that children with and without dyslexia can benefit in similar ways from the multi-modal, nonverbal cues implemented in the training software. Children with dyslexia are characterized by

poor phonological awareness, which is attributed to difficulties in memorizing the sound-symbol associations. Since it is known that individuals with dyslexia use a nonphonological, visual coding strategy for memorizing information (Miller et al., 2009), we linked the culturally determined association between sound and letter with a nonverbal visual code. Therefore, individuals with dyslexia are faced with a naturally occurring visual coding strategy that facilitates the memorization of the word form.

Our data analysis points out that although children with and without dyslexia might have different memorizing strategies, as proposed by Miller and Kupfermann (2009), both groups were able to form 'memory traces' in long term-memory for orthography and general orthographic rules based on the German language. It has been suggested that it is more effective to teach children with reading difficulties the phoneme-grapheme correspondence by employing a method that models connections between written and spoken words, as opposed to using a phonics rule based approach (Berninger et al., 1999). These modeled connections support to create associative links between orthographic input representations and phonological output representations. Thus, repeated presentations of orthographic forms drive phonological responses. Berninger and colleagues (1999) state that when explicit modeling of spelling-sound connections for multi-letter spelling units are taught from the beginning of formal instructions in reading, confusion can be avoided. Additionally, they assume that children with impaired phonological or orthographic awareness might benefit from color coded spelling units (Berninger et al., 1999).

Further Analysis

In a further step we aimed to identify the cognitive abilities responsible for acquiring spelling performances. We assume that successful learning is guided by attention and memorizing performances. Accordingly, we analyzed different attention functions (alertness, flexibility, and impulse control), as well as memory performances (learning progress, short-term memory functions, and long-term memory functions), in order to examine which cognitive components affect the acquiring of spelling skills. Respectively, our analyses demonstrate that children benefit from the structured learning environment of the learning software.

Attention Functions

Generally, we found that children with low vs. high attention scores (impulse control, flexibility, and alertness) committed significantly more spelling errors at the beginning of the training. These findings indicate that low scorers had not benefited as much from traditional teach-

ing and schooling in orthography as high scorers; however, both groups (low and high attention scores) benefited from the computer-based training to the same extent. In addition, the same skill level could be expected to be seen in both groups as a result of this training.

We suggest that working on the computer facilitates children to structure their working strategy and supports them with focusing on the relevant task. The structural guidance is enforced with the interface of the topological code, which assists the users in their serial behavior of putting the correct letters in the right position. The support with focusing the attention on the relevant stimulus might be beneficial for children with reduced attention functions. Our findings are in line with previous evidence that children with ADHD can also improve their spelling skills when a clear strategy is taught (Re, Caeran, & Cornoldi, 2008).

Memory Functions

In our analysis of spelling curves we aimed to examine the influence of memory performances on spelling skills. Our data indicates that children with high and low memory performance start at the same spelling level and will reach the same limit at the end of the study. However, children with high (vs. low) verbal learning progress and short- and long-term memory scores benefited significantly more from the computer based training. These results are consistent with the notion that children's abilities to store and manipulate information in complex memory performances may have strong influence on learning; furthermore, these abilities may be associated with scholastic attainment during their school career (Gathercole, Alloway, Willis, & Adams, 2006). Children with poor verbal memory skills; therefore, show specific impairments in the process of learning the phonological structures of new vocabulary items (Baddeley, Gathercole, & Papagno, 1998). Long-term memory can be considered a crucial cognitive function that subserves phonological, grapheme, and lexical representations. Consequently, long-term memory has a strong influence on learning reading and spelling skills.

Comparatively, our data evidences that children with high memory performance benefited greatly from the information provided by the learning software as it strengthens the retrieval of letters or phonemes stored in memory structures.

Limitations and Further Research

Our data are collected by a computer-based training program that supports children's spelling behavior by using visual and auditory codes. The transfer to a paper-pencil test is not demonstrated in the present work because we demonstrated previously (Kast et al., 2007) that both

children with and without dyslexia could improve their spelling skills. Spelling improvements were observed for both learned and non-learned words.

The software presented in the current study permits children to work independently according to their own learning pace. Since the software adapts to the individual level, it can be considered as a complement to traditional teacher supervised learning. The presently available data implies that this training should also be effective in a classroom setting, if the infrastructure (enough computers) is available. Nevertheless, working with a computer neglects important influences on social and emotional aspects on learning.

Although children with dyslexia benefit from the information provided by the actual version of the learning software, the data show that they still do not reach the same level as children without dyslexia. treatment of DD is longstanding and further training is needed. Since children with low reading and spelling skills have to work hard to improve their orthographic knowledge, motivation has a great impact on learning behavior. To maintain children's motivation to continue the training, which in turn may result in enhanced spelling skills, the provision of external and internal rewards might play a crucial role. Hence, it would be of interest to further investigate motivational aspects that may be involved by implementing different rewarding systems in the learning software. Provision of rewards, as well as the resulting motivation should be examined in relation to personality traits.

Conclusion

In summary, our results demonstrate that the additional textural cue, visualization of the phonemes, and the new phoneme-based word selection controller, which were adapted to individual difficulties, positively influenced the spelling performance of children with dyslexia. Additionally, there is evidence that both children with and without dyslexia profit from the computer based training in a similar way. Both groups were able to use the visual and auditory coding system implemented in the learning software to acquire spelling skills. Children with dyslexia were able to strengthen their memories of grapheme to phoneme correspondence. As a result, we suggest that abstract visual and auditory cues facilitated the memorization of phonological information. Similarly, children with low (vs. high) attentional performances could benefit equally from the structured computer-based learning software. This finding implicates that children with low attention resources need clear guidance and may benefit from a structured methodological approach. Moreover, we were able to show that the usage of information cues requires memory skills. In addition, memory functions correlate positively with

learning progress irrespective of dyslexia. This indicates that memory functions are important cognitive sources for acquiring spelling skills.

Acknowledgment

This project was supported by the Research Funding University of Zurich (56234102), the SNF-grant 320000 – 120661/1, and the CTI-grant 8970.1.

9 General Discussion

The present work aimed to investigate the functional and behavioral correlates of DD. It is known that established phoneme to grapheme conversion is essential for reading and spelling behavior. For this purpose we designed four different studies to especially examine the phoneme to grapheme mapping in dyslexic children and adults, during word decoding. Additionally, we investigated the spelling behavior of children working with a learning software that provides phoneme-based information to aid in the acquiring of spelling skills.

In general visually presented stimuli are eliciting reliable electrical potentials over occipito-temporal regions. Visually presented words, pseudowords, strings of consonants and strings of alphanumeric symbols evoke a sharp negative going peak approximately 170 ms after onset (Bentin et al., 1999; Rossion et al., 2003). This N170 or 'pre-lexical component' reflects the conjunction of letters into the integrated visual percept (phoneme to grapheme conversion) (Maurer et al., 2005) and the experience-dependent neural changes of visual expertise (Nobre et al., 1994). In accordance with this theoretical framework, our first experiment design investigated dyslexic and non-dyslexic children utilizing a lexical decision task between words and pseudowords (see Appendix for a full list of stimuli used).
In the results of the first study we observed, over occiptio-temporal electrodes, decreased N170 amplitudes for dyslexic compared to non-dyslexic children. Reduced N170 amplitudes in dyslexic children were found bilaterally for pseudowords and on the left hemisphere for words. This indicates that dyslexic children show less activation in a component sensitive for processing print, which develops as a function of accumulated experience. Additionally, our data evidenced that, irrespective of group, words and pseudowords are bilaterally processed in children. In contrast, studies examining adults while performing reading tasks revealed a left lateralized N170 (Maurer et al., 2008b; Nobre et al., 1994; Rossion et al., 2003). The absence of the clear left hemispheric processing dominance for print in both dyslexic and non-dyslexic children supports the assumption that asymmetric language processing is a function of maturation (McCandliss et al., 2003b) and experience (Aghababian et al., 2000; Spironelli et al., 2009). It has been suggested that there is no ready-made 'module' for visual word recognition but rather a progressive specialization process that activates plasticity of the leftward human ventral inferiotemporal cortex, building up the visual word form area (VWFA) (Cohen et al., 2004).

The data of our second study revealed that dyslexics displayed, when compared to non-dyslexic adults, stronger mean amplitudes of the global field power (GFP) in a TW overlapping with the N170 component, specifically during the processing of visually presented disyllabic nouns. While the N170 in non-reading kindergarten children was absent, this component emerged in less than two years of reading experience (Maurer et al., 2006). Additionally, it is known that skilled readers show increased activity over the leftward occiptio-temporal regions (McCandliss et al., 2003b), while word-forms are, in dyslexic adults, instead processed less lateralized (Helenius et al., 1999). Hence, our data evidence that dyslexic adults recruit a larger and wider neuronal network over the global head while performing phoneme to grapheme mapping, to compensate for the reduced neuronal responses over posterior areas. This in line with the finding of a previously published MEG study (Helenius et al., 1999) that presented the persistence of disturbed electrophysiological responses for word decoding into adulthood.

Word decoding relies on an audiovisual process, whereas the purely visually processed orthography has to be transformed in the phonological representation (Ehri et al., 1980; Ziegler et al., 2005). The efficient association of orthographical and phonological information is, in skilled readers, considered to be an over-learned process (van Atteveldt et al., 2007a) which occurs rapidly and automatically (Paulesu et al., 1996). Dyslexics, however, struggle with acquiring phoneme to grapheme mapping skills, and with the establishment of an efficient letter to speech-sound association, which is essential for word decoding. Efficient phoneme to grapheme mapping may never be fully obtained (Vellutino et al., 2004). These culturally unique defined phoneme to grapheme associations rely on an audiovisual (AV) processing mechanism similar to the integration of speech (Raij et al., 2000; van Atteveldt et al., 2004). According to this assumption, we used EEG- and fMRI experiments to examine the neural mechanism sub-serving audiovisual integration of phonological information in dyslexic and non-dyslexic adults. In the EEG experiment disyllabic German nouns (see for uses stimuli Appendix) were presented to our subjects unimodally (auditorily, visually) or audiovisually (congruent or incongruent). In the context of the fMRI study we used disyllabic German words and pseudowords that were presented auditorily (A), visually (V) or audiovisually (AV).

Within a late time window (occurring approximately 400 ms after stimulus onset), the EEG study revealed enhanced mean amplitudes of the GFP in dyslexic compared to non-dyslexic adults. This finding was observed for both the audiovisual congruent (AVc) and the audiovisual incongruent (AVi) conditions. This indicates that dyslexic compared to non-dyslexic

adults differ in their recruitment of neuronal circuits in response to AV presented phonological information. Additionally, it leads to the suggestion of an impaired AV integration mechanism in dyslexic adults, specifically in the TW overlapping with N400.

The inverse effectiveness rule (Meredith et al., 1983) states that the pairing of weakly effective stimuli (those that are difficult to perceive or identify) results in a vigorous enhancement of the bimodal neuronal activity, while the combination of highly effective stimuli causes little increase in the neural response. In line with this theoretical framework the increased neuronal response observed in dyslexic adults might reflect dysfunctional unisensory processing that result in increased activation in bimodal areas. It could be that the enhanced N170 we observed for the visual condition in dyslexic compared to non-dyslexic adults could influence the AV processing in a later TW. This notion is in accorcance to the assumption of the feedforward mechanism in AV integration (Driver et al., 2008).

Alternatively, the enhanced neuronal response revealed for dyslexic compared to non-dyslexic adults can be explained by the neuronal efficient hypothesis (NEH). This theory claims that lower and more focused cortical activation reflects higher neural efficiency and preferentially occurs in experts (Micheloyannis et al., 2006). Due to the fact that non-dyslexic compared to dyslexic adults are characterized by greater proficiency in word decoding and spelling, skilled readers process phonological information more efficiently and recruit a smaller neuronal network.

The electrophysiological response at about 400 ms after stimulus onset is associated with language related functions and reflects AV integration of semantic information. Processing semantic informaiton in linguistic contexts is associated with the N400 component (Kutas et al., 1980). This component is dependent on the immediate context in which it occurs. It has also been observed in previous studies investigating the integration of AVc and AVi stimuli with a more negative going ERP response for the AVi condition at about 390ms after stimulus onset (Molholm et al., 2004). In our data this incongruency effect in the GFP of the ERP did not differ between groups. However, our data evidence group differences in the topographic maps for the AVi condition 408-432ms after stimulus onset. This finding might reflect a different proficiency for integrating semantic information between dyslexic and non-dyslexic individuals. Due to the intact phonological system of non-dyslexic adults words might be better represented in the semantic lexicon, whereas dyslexic adults might show less sensitivity to this kind of semantic violation. This reasoning is supported by the phonological deficit theory (Bradley et al., 1983; Ramus et al., 2003b).

The data of the fMRI experiment revealed stronger hemodynamic responses for non-dyslexic compared to dyslexic adults in the left hemispheric supramargnial gyurs (SMG) as well as on the right side in the superior temporal sulcus (STS), irrespective of condition (A, V, AV) or stimuli (words, pseudowords). It has been suggested that the SMG plays an important role in the perception and production of phonemes (Caplan et al., 1995; Ojemann et al., 1989) as well in providing cross-modal relation of auditory and visual processing during reading (Gabrieli, 2009). The SMG and angular gyurs (AG) have been considered to play a pivotal role in transforming the orthographic representation in the phonological representation of the language system (Damasio et al., 1983). In line with this assumption, our data indicate that the SMG might function as important relay stations processing linguistic stimuli from different modalities and might therefore integrate the audiovisual information, which is essential for phoneme to grapheme mapping and thus for decoding written words. Therefore, we assume that the reduced hemodynamic response of the dyslexic individuals in the leftward SMG reflects reduced phoneme to grapheme mapping skills.

The STS has previously been considered as a multimodal area that receives visual, somatosensoy and auditory information in monkeys (Seltzer et al., 1994) and in humans (Beauchamp et al., 2004). Notably, the STS integrates AV presented speech and non-speech stimuli (Beauchamp, 2005; Calvert et al., 2000; Miller et al., 2005; Sekiyama et al., 2003). Previous fMRI studies examined AVc and AVi integration of graphemes to phonemes in dyslexic adults (Blau et al., 2009) and dyslexic children (Blau et al., 2010). Dyslexic readers failed to modulate the response to speech sounds when those sounds were presented together with visual letters for both conditions AVc and AVi on the bilateral STS. The authors interpreted these findings as an impaired integration mechanism of letter to speech-sounds in dyslexic adults (Blau et al., 2009). In line with this interpretation we assume that the reduced hemodynamic response in a multisensory region indicates that the audiovisual integration of phoneme to graphemes (which is essential for word and pseudoword decoding) might be impaired in dyslexic individuals.

Significantly, our fMRI data yielded a significant group by condition interaction in the anterior insula on the right hemisphere. Whereas non-dyslexic adults show enhanced hemodynamic responses for the auditory condition, dyslexic adults demonstrate stronger BOLD signals for the visual and audiovisual condition. Additionally, our data revealed a positive correlation between activity relating spelling skills, and auditorily presented words and pseudowords in the rightward insula. Therefore, our findings indicate that the reduced activity in the rightward insula during auditory stimulation of word-like stimuli in DD is, to some degree, associated

with an auditory deficit. Beyond the involvement in several auditory functions, the insula has previously been considered as intermediate site between a primary sensory area and a high order association area that integrates auditory information with other associative functions (Bushara et al., 2001; Lewis et al., 2000). Hence, the right hemispheric insula has previously be pointed out a as a multimodal integration area that responds to visual, tactile and auditory stimuli (anterior > posterior), although the activation was less prominent than in other multimodal areas such as the right temporoparietal junction (Bamiou et al., 2003). We therefore assume that the revealed group by condition interaction may reflect aberrant integration processes of auditorily presented phonological information and other associative functions in the visual domain. This, in turn, may cause phonological processing impairments, namely poor phoneme to grapheme mapping.

Taken together, word decoding is a bimodal task which requires that the orthographic representation (grapheme) has to be transformed to the phonological representation (phoneme). Established phoneme to grapheme knowledge is essential for reading and spelling (Byrne, 1998). Previous studies revealed reduced phoneme to grapheme mapping skills in dyslexic individuals (Bryne, 1998; Vellutino e al., 2004). Our studies evidenced that dyslexic compared to non-dyslexic adults recruit neuronal circuits specialized for processing phonological information differently. To date the underlying mechanism is not fully understood. It is possible that impairments in one unisensory modality influence the other modality. The neuronal interaction of these unisensory areas may cause abnormal responses in the multisensory regions. Hence, it could be that these unusual responses in multimodal areas are responsible for the deficient phoneme to grapheme mapping and, in turn, for the reading difficulties.
The EEG data evidenced that dyslexic individuals showed an enhanced electrophysiological response during the visual condition (word decoding) in a TW sensitive for phonological processing, i.e. phoneme to grapheme mapping. This might reflect compensating mechanism due to reduced neuronal responses over posterior areas. The fMRI data revealed in the rightward insula a group by condition interaction with reduced neuronal response for the auditory compared to audiovisual and visual condition, which leads to the suggestion that this reflects auditory processing deficit of phonological information in dyslexic adults. Therefore, it could be that these unisensory impairments caused aberrant responses in multisensory areas responsible for phonological processing. Alternatively, it could be that dyslexic individuals placed due to deficient neural migration per se less neurons in multisensory areas sensitive to

processing phonological information, which in turn causes impaired phoneme to grapheme conversion and therefore reading problems.

The previously mentioned experiments provided evidence that DD is associated with a phonological deficit. Accordingly, a computer based spelling program for dyslexic children expanded the framework of the learning software by adding two phoneme- based adjustments. One adaption was the implementation of an additional non-verbal phonological cue. This cue visualized the catenation of multiple letters to one grapheme representing the corresponding phoneme (e.g. sch, ch, ie, ei). The other adjustment was the realization of a new selection controller reflecting a phoneme-based student model (Baschera et al., 2009), and which allows for an adaption to account for individual spelling difficulties. This spelling tutor software recoded words into multi-sensory non-verbal representations comprising meaningful visual and auditory codes. These original codes represented letter and syllable based information. In a comprehensive pilot study we demonstrated that children irrespective of group reduced their spelling mistakes about 30 % after working for three months with the original multi-modal spelling program (Kast et al., 2007). The aim of the forth experiment was to improve the spelling software. The data of the forth experiment compared children using two versions of the software: dyslexic children working with a second, adapted training-system were compared to dyslexic children training with the first and original software version. The dyslexic children working with the second version were able to improve their spelling by +154%, a significant change in their spelling behavior. Due to the fact that the dyslexic children from both the first and the second study show comparable initial and asymptotic error probabilities on phoneme to grapheme mapping (PGM), we suggest that the two groups did not differ per se. Rather it indicates that the phoneme based adjustments of the learning software supported the children in their spelling behavior. We assume that the easily extractable information about the phonological word structure, which was linked with a further non-verbal visual cue, facilitated the memorizing of the phoneme to grapheme mapping and therefore the word-form.
Another important factor responsible for the enhancement of the spelling skills was the phoneme-based word selection controller. This controller identifies the children's individual difficulties based on their error behavior and prompts words containing these problems. In contrast to the old word selection method which relies on a letter-based analysis of errors, the new controller accounts for spelling difficulties on a phonological level. The child is repeatedly confronted with his/her individual spelling challenges. Consequently the child learns the

linguistic spelling rules based on the German language and generalizes them to other words after training.

Our data also demonstrated that the multi-modal training (i.e. the second software version) induced a significant decrease of spelling errors, particularly in PGM, for both dyslexic and non-dyslexic children. Finding the same learning curve in both groups indicates that dyslexic and non-dyslexic children can benefit in similar ways from the multi-modal, non-verbal cues implemented in the training software. This evidences that dyslexic children also can learn the phoneme to grapheme mapping essential for spelling when they receive adequate treatment. The underlying concept of the software used in the present study is to mimic the dyslexic individuals' naturally occurring visual coding strategy. Previous findings demonstrate that dyslexic children use a visual coding strategy whereas non-dyslexic children use phonological coding strategy to maintain information in the working memory (Miller et al., 2009). However, abstract visual and auditory non-verbal codes implemented by this learning software are used to teach the sound-symbol association of words. This is in line with the findings of previous studies revealing that dyslexics have difficulties in learning the culturally defined phoneme to grapheme correspondence (Vellutino et al., 2004) or learning the association of an abstract form with non-sense syllables (Gascon et al., 1970; Vellutino et al., 1975). Contrarily, dyslexics performed normally on non-verbal paired association tasks such as learning to associate one abstract shape with another (Goyen et al., 1971; Vellutino et al., 1975). We assume that children with impaired phonological awareness might benefit from this multimodal non-verbal coding system for acquiring spelling skills.

In a further step, we aimed to identify the cognitive architecture responsible for acquiring spelling performances. We assume that successful learning is guided by attention and memory performances. Hence, we analyzed attention functions as well as memory performances to examine which cognitive components affect the acquiring of spelling skills. Respectively, our analyses demonstrate which children benefit from the structured learning environment of the learning software.

Our data demonstrated that children with low compared to high attention scores committed significantly more spelling errors at the beginning of the training. These findings indicate that low scorers cannot benefit as much from traditional teaching and schooling in orthography as high scorers. However, both groups (low and high attention scores) benefited from the computer-based training to the same extent, and even the same skill level could be expected from this training. We suggest that working on the computer helps children to structure their working strategy and supports them in focusing on the relevant task. The structural guidance is

enforced with the interface of the topological code, which supports the users in their serial behavior of putting the correct letters in the right position. The support in focusing the attention on the relevant stimulus might be particularly beneficial for children with reduced attention functions.
Additionally, our data indicates that children with high (vs. low) memory scores benefit significantly more from the computer based training. This finding evidences that children with high memory performances benefit greatly from the information provided by the learning software and strengthens the retrieval of letters or phonemes stored in memory structures.

Taken together, our findings demonstrate that the two phoneme-based adjustments influenced the dyslexic children positively on in their spelling performances. Additionally, there is evidence that both dyslexic and non-dyslexic children profit from the computer based training in a similar way. Both groups were able to use the visual and auditory coding system implemented in the learning software for acquiring spelling skills. Dyslexic children could strengthen memories of grapheme to phoneme correspondence, and we suggest that abstract visual and auditory cues helped them in memorizing the phonological information.
More generally our data evidence that treatments in dyslexic individuals can be fruitful. Interventions based on acquiring phoneme to grapheme mapping skills by using non-verbal visual and auditory codes supports them in memorizing the word-forms correctly.

Conclusions

Several decades of research into DD has created a plethora of studies. These studies have been conducted representing various theoretical approaches and differing applied methods. In spite of this richness of research into the underlying pathomechanism, its complexity is still not fully understood. To date the phonological deficit hypothesis is one of the most accepted theoretical frameworks in the field of DD and our data do support this approach even though deficits that might occur in the auditory, visual or motorsensory system can not be explained by this theory. Due to the heterogenous pathomechanism it can not be the goal of this work to clarify all the open questions and unravel the exact neuronal disorder. Even though the PhD thesis can not be considered an ultimate explanation that revealed fully the nature of DD it makes a strong and compelling argument in favour of phonological deficit theory. Based on the evidence provided by this thesis we conclude that to date investigators have too much focused on the unisensory deficits and ignored the issue of multisensory processing of phono-

logical information in dyslexic individuals. Nevertheless, further research is still needed to gain more information about the multisensory integration of phonologicial contents in dyslexic individuals, and about the interaction of unisensory and multisensory systems.

10 References

Ackermann, H., & Riecker, A. (2004). The contribution of the insula to motor aspects of speech production: a review and a hypothesis. *Brain Lang, 89*(2), 320-328.

Ackermann, H., & Riecker, A. (2010). The contribution(s) of the insula to speech production: a review of the clinical and functional imaging literature. *Brain Struct Funct, 214*(5-6), 419-433.

Adams, M. J. (1990). *Beginning to read: Thinking and learning about print*. Cambridge MA: MIT Press.

Aghababian, V., & Nazir, T. A. (2000). Developing normal reading skills: aspects of the visual processes underlying word recognition. *J Exp Child Psychol, 76*(2), 123-150.

Akaike, H. (1974). A new look at the statistical model identification. *Automatic Control, IEEE Transactions on, 19*, 716-723.

Amitay, S., Ahissar, M., & Nelken, I. (2002a). Auditory processing deficits in reading disabled adults. *J Assoc Res Otolaryngol, 3*(3), 302-320.

Amitay, S., Ben-Yehudah, G., Banai, K., & Ahissar, M. (2002b). Disabled readers suffer from visual and auditory impairments but not from a specific magnocellular deficit. *Brain, 125*(Pt 10), 2272-2285.

Annett, M. (1970). A Classification of Hand Preferences by Association Analysis. *British Journal of Psychology, 61*, 303-321.

Asbjornsen, A. E., & Bryden, M. P. (1998). Auditory attentional shifts in reading-disabled students: quantification of attentional effectiveness by the Attentional Shift Index. *Neuropsychologia, 36*(2), 143-148.

Aylward, E. H., Richards, T. L., Berninger, V. W., Nagy, W. E., Field, K. M., Grimme, A. C., Richards, A. L., Thomson, J. B., & Cramer, S. C. (2003). Instructional treatment associated with changes in brain activation in children with dyslexia. *Neurology, 61*(2), 212-219.

Bach, S., Brandeis, D., Hofstetter, C., Martin, E., Richardson, U., & Brem, S. (2010). Early emergence of deviant frontal fMRI activity for phonological processes in poor beginning readers. *Neuroimage, 53*(2), 682-693.

Baddeley, A., Gathercole, S., & Papagno, C. (1998). The phonological loop as a language learning device. *Psychol Rev, 105*(1), 158-173.

Baldeweg, T., Richardson, A., Watkins, S., Foale, C., & Gruzelier, J. (1999). Impaired auditory frequency discrimination in dyslexia detected with mismatch evoked potentials. *Ann Neurol, 45*(4), 495-503.

Bamiou, D. E., Musiek, F. E., & Luxon, L. M. (2003). The insula (Island of Reil) and its role in auditory processing. Literature review. *Brain Res Brain Res Rev, 42*(2), 143-154.

Baschera, G. M., & Gross, M. (2009). *A Phoneme-Based Student Model for Adaptive Spelling Training.* Paper presented at the In Proceedings of Artificial Intelligence in Education.

Bauer, M. (2008). Multisensory integration: a functional role for inter-area synchronization? *Curr Biol, 18*(16), R709-710.

Baxter, D. M., & Warrington, E. K. (1985). Category specific phonological dysgraphia. *Neuropsychologia, 23*(5), 653-666.

Bear, M. F. (1996). A synaptic basis for memory storage in the cerebral cortex. *Proc Natl Acad Sci U S A, 93*(24), 13453-13459.

Beauchamp, M. S., Argall, B. D., Bodurka, J., Duyn, J. H., & Martin, A. (2004). Unraveling multisensory integration: patchy organization within human STS multisensory cortex. *Nat Neurosci, 7*(11), 1190-1192.

Beauchamp, M. S. (2005). See me, hear me, touch me: multisensory integration in lateral occipital-temporal cortex. *Curr Opin Neurobiol, 15*(2), 145-153.

Beneventi, H., Tonnessen, F. E., Ersland, L., & Hugdahl, K. (2010). Executive working memory processes in dyslexia: Behavioral and fMRI evidence. *Scand J Psychol*.

Benevento, L. A., Fallon, J., Davis, B. J., & Rezak, M. (1977). Auditory--visual interaction in single cells in the cortex of the superior temporal sulcus and the orbital frontal cortex of the macaque monkey. *Exp Neurol, 57*(3), 849-872.

Bentin, S., Allison, T., Puce, A., Perez, E., & McCarthy, G. (1996). Electrophysiological Studies of Face Perception in Humans. *Journal of Cognitive Neuroscience, 8*(6), 551-565.

Bentin, S., Mouchetant-Rostaing, Y., Giard, M. H., Echallier, J. F., & Pernier, J. (1999). ERP manifestations of processing printed words at different psycholinguistic levels: time course and scalp distribution. *J Cogn Neurosci, 11*(3), 235-260.

Bentin, S., Taylor, M. J., Rousselet, G. A., Itier, R. J., Caldara, R., Schyns, P. G., Jacques, C., & Rossion, B. (2007). Controlling interstimulus perceptual variance does not abolish N170 face sensitivity. *Nat Neurosci, 10*(7), 801-802; author reply 802-803.

Berninger, V. W., Abbott, R. D., Zook, D., Ogier, S., Lemos-Britton, Z., & Brooksher, R. (1999). Early Intervention for Reading Disabilities. *Journal of Learning Disabilities, 32*(6), 491-503.

Berninger, V. W., Abbott, R. D., Jones, J., Wolf, B. J., Gould, L., Anderson-Youngstrom, M., Shimada, S., & Apel, K. (2006). Early development of language by hand: composing, reading, listening, and speaking connections; three letter-writing modes; and fast mapping in spelling. *Developmental Neuropsychology, 29*(1), 61-92.

Bishop, D. V. (2002). Cerebellar abnormalities in developmental dyslexia: cause, correlate or consequence? *Cortex, 38*(4), 491-498.

Blau, V., van Atteveldt, N., Ekkebus, M., Goebel, R., & Blomert, L. (2009). Reduced neural integration of letters and speech sounds links phonological and reading deficits in adult dyslexia. *Curr Biol, 19*(6), 503-508.

Blau, V., Reithler, J., van Atteveldt, N., Seitz, J., Gerretsen, P., Goebel, R., & Blomert, L. (2010). Deviant processing of letters and speech sounds as proximate cause of reading failure: a functional magnetic resonance imaging study of dyslexic children. *Brain, 133*(Pt 3), 868-879.

Bodén, M., & Bodén, M. (2007). Evolving spelling exercises to suit individual student needs. *Applied Sort Computing, 7*, 126-135.

Bodner, M., Kroger, J., & Fuster, J. M. (1996). Auditory memory cells in dorsolateral prefrontal cortex. *Neuroreport, 7*(12), 1905-1908.

Boemio, A., Fromm, S., Braun, A., & Poeppel, D. (2005). Hierarchical and asymmetric temporal sensitivity in human auditory cortices. *Nat Neurosci, 8*(3), 389-395.

Bolger, D. J., Perfetti, C. A., & Schneider, W. (2005). Cross-cultural effect on the brain revisited: universal structures plus writing system variation. *Hum Brain Mapp, 25*(1), 92-104.

Booth, J. R., Burman, D. D., Meyer, J. R., Lei, Z., Choy, J., Gitelman, D. R., Parrish, T. B., & Mesulam, M. M. (2003). Modality-specific and -independent developmental differences in the neural substrate for lexical processing. *J Neurolinguistics, 16*(4-5), 383-405.

Bosch, V. (2000). Statistical analysis of multi-subject fMRI data: assessment of focal activations. *J Magn Reson Imaging, 11*(1), 61-64.

Bowers, P. G., & Swanson, L. B. (1991). Naming speed deficits in reading disability: multiple measures of a singular process. *J Exp Child Psychol, 51*(2), 195-219.

Bradley, L., & Bryant, P. E. (1983). Categorizing sounds and learning to read-a causal connection. *Nature, 301*, 419-421.

Breier, J. I., Gray, L., Fletcher, J. M., Diehl, R. L., Klaas, P., Foorman, B. R., & Molis, M. R. (2001). Perception of voice and tone onset time continua in children with dyslexia with and without attention deficit/hyperactivity disorder. *J Exp Child Psychol, 80*(3), 245-270.

Brem, S., Bach, S., Kucian, K., Guttorm, T. K., Martin, E., Lyytinen, H., Brandeis, D., & Richardson, U. (2010). Brain sensitivity to print emerges when children learn letter-speech sound correspondences. *Proc Natl Acad Sci U S A, 107*(17), 7939-7944.

Brem, S., Bucher, K., Halder, P., Summers, P., Dietrich, T., Martin, E., & Brandeis, D. (2006). Evidence for developmental changes in the visual word processing network beyond adolescence. *Neuroimage, 29*(3), 822-837.

Brindley, G. S. (1964). The use made by the cerebellum of the information that it receives from the sense organs. *IBRO Bulletin, 3*, 80.

Brunswick, N., McCrory, E., Price, C. J., Frith, C. D., & Frith, U. (1999). Explicit and implicit processing of words and pseudowords by adult developmental dyslexics: A search for Wernicke's Wortschatz? *Brain, 122 (Pt 10)*, 1901-1917.

Bryne, B. (1998). *The fondation of literacy: The child's acquistion of the alphabetic principle*. East Sussex UK: Psychology Press.

Bundo, M., Kaneoke, Y., Inao, S., Yoshida, J., Nakamura, A., & Kakigi, R. (2000). Human visual motion areas determined individually by magnetoencephalography and 3D magnetic resonance imaging. *Hum Brain Mapp, 11*(1), 33-45.

Bushara, K. O., Grafman, J., & Hallett, M. (2001). Neural correlates of auditory-visual stimulus onset asynchrony detection. *J Neurosci, 21*(1), 300-304.

Byrne, B. (1998). *The foundation of literacy: The child's acquistion of the alphabetic principle*. East Sussex UK: Psychology Press.

Calvert, G. A., Brammer, M. J., Bullmore, E. T., Campbell, R., Iversen, S. D., & David, A. S. (1999). Response amplification in sensory-specific cortices during crossmodal binding. *Neuroreport, 10*(12), 2619-2623.

Calvert, G. A., Campbell, R., & Brammer, M. J. (2000). Evidence from functional magnetic resonance imaging of crossmodal binding in the human heteromodal cortex. *Curr Biol, 10*(11), 649-657.

Calvert, G. A., & Thesen, T. (2004). Multisensory integration: methodological approaches and emerging principles in the human brain. *J Physiol Paris, 98*(1-3), 191-205.

Caplan, D., Gow, D., & Makris, N. (1995). Analysis of lesions by MRI in stroke patients with acoustic-phonetic processing deficits. *Neurology, 45*(2), 293-298.

Cardon, L. R., Smith, S. D., Fulker, D. W., Kimberling, W. J., Pennington, B. F., & DeFries, J. C. (1994). Quantitative trait locus for reading disability on chromosome 6. *Science, 266*(5183), 276-279.

Carreiras, M., Mechelli, A., Estevez, A., & Price, C. J. (2007). Brain activation for lexical decision and reading aloud: two sides of the same coin? *J Cogn Neurosci, 19*(3), 433-444.

Castles, A., & Coltheart, M. (1993). Varieties of developmental dyslexia. *Cognition, 47*(2), 149-180.

Caylak, E. (2009). Neurobiological approaches on brains of children with dyslexia: review. *Acad Radiol, 16*(8), 1003-1024.

Cestnick, L. (2001). Cross-modality temporal processing deficits in developmental phonological dyslexics. *Brain Cogn, 46*(3), 319-325.

Coch, D., & Holcomb, P. J. (2003). The N400 in beginning readers. *Developmental Psychobiology, 43*(2), 146-166.

Cohen, L., Dehaene, S., Naccache, L., Lehericy, S., Dehaene-Lambertz, G., Henaff, M. A., & Michel, F. (2000). The visual word form area: spatial and temporal characterization of an initial stage of reading in normal subjects and posterior split-brain patients. *Brain, 123 (Pt 2)*, 291-307.

Cohen, L., Lehericy, S., Chochon, F., Lemer, C., Rivaud, S., & Dehaene, S. (2002). Language-specific tuning of visual cortex? Functional properties of the Visual Word Form Area. *Brain, 125*(Pt 5), 1054-1069.

Cohen, L., & Dehaene, S. (2004). Specialization within the ventral stream: the case for the visual word form area. *Neuroimage, 22*(1), 466-476.

Coltheart , M., Patterson, K. E., & Marshall, J. C. (1980). *Deep dyslexia*. London: Routleged and Kegan Paul.

Coltheart, M., Curtis, B., Atkins, P., & Haller, M. (1993). Models of Reading Aloud: Dual-Route and Parallel-Distributed-Processing Approaches. *Psychological Review, I00*, 589-608.

Coltheart, M., Rastle, K., Perry, C., Langdon, R., & Ziegler, J. (2001). DRC: a dual route cascaded model of visual word recognition and reading aloud. *Psychol Rev, 108*(1), 204-256.

Cope, N., Harold, D., Hill, G., Moskvina, V., Stevenson, J., Holmans, P., Owen, M. J., O'Donovan, M. C., & Williams, J. (2005). Strong evidence that KIAA0319 on chromosome 6p is a susceptibility gene for developmental dyslexia. *Am J Hum Genet, 76*(4), 581-591.

Corina, D. P., Richards, T. L., Serafini, S., Richards, A. L., Steury, K., Abbott, R. D., Echelard, D. R., Maravilla, K. R., & Berninger, V. W. (2001). fMRI auditory language differences between dyslexic and able reading children. *Neuroreport, 12*(6), 1195-1201.

Cornelissen, P., Bradley, L., Fowler, S., & Stein, J. (1991). What children see affects how they read. *Dev Med Child Neurol, 33*(9), 755-762.

Cornelissen, P., Richardson, A., Mason, A., Fowler, S., & Stein, J. (1995). Contrast sensitivity and coherent motion detection measured at photopic luminance levels in dyslexics and controls. *Vision Res, 35*(10), 1483-1494.

Cornelissen, P. L., Hansen, P. C., Bradley, L., & Stein, J. F. (1996). Analysis of perceptual confusions between nine sets of consonant-vowel sounds in normal and dyslexic adults. *Cognition, 59*(3), 275-306.

Cornelissen, P., Tarkiainen, A., Helenius, P., & Salmelin, R. (2003). Cortical effects of shifting letter position in letter strings of varying length. *J Cogn Neurosci, 15*(5), 731-746.

Damasio, A. R., & Damasio, H. (1983). The anatomic basis of pure alexia. *Neurology, 33*(12), 1573-1583.

de Jong, P. F. (1998). Working memory deficits of reading disabled children. *J Exp Child Psychol, 70*(2), 75-96.

De Martino, S., Espesser, R., Rey, V., & Habib, M. (2001). The "temporal processing deficit" hypothesis in dyslexia: new experimental evidence. *Brain Cogn, 46*(1-2), 104-108.

Dehaene, S., Le Clec, H. G., Poline, J. B., Le Bihan, D., & Cohen, L. (2002). The visual word form area: a prelexical representation of visual words in the fusiform gyrus. *Neuroreport, 13*(3), 321-325.

Dehaene, S., Cohen, L., Sigman, M., & Vinckier, F. (2005). The neural code for written words: a proposal. *Trends Cogn Sci, 9*(7), 335-341.

Dejerine, J. (1891). Sur un cand de cécité verbale aved agraphie, suivi d'autopsie. *Mém Soc Biol, 3*, 197-201.

Del Percio, C., Rossini, P. M., Marzano, N., Iacoboni, M., Infarinato, F., Aschieri, P., Lino, A., Fiore, A., Toran, G., Babiloni, C., & Eusebi, F. (2008). Is there a "neural efficiency" in athletes? A high-resolution EEG study. *Neuroimage, 42*(4), 1544-1553.

Demonet, J. F., Taylor, M. J., & Chaix, Y. (2004). Developmental dyslexia. *Lancet, 363*(9419), 1451-1460.

Deutsch, G. K., Dougherty, R. F., Bammer, R., Siok, W. T., Gabrieli, J. D., & Wandell, B. (2005). Children's reading performance is correlated with white matter structure measured by diffusion tensor imaging. *Cortex, 41*(3), 354-363.

Di Russo, F., Pitzalis, S., Aprile, T., & Spinelli, D. (2005). Effect of practice on brain activity: an investigation in top-level rifle shooters. *Med Sci Sports Exerc, 37*(9), 1586-1593.

Drewe, E. A. (1975). Go-nogo learning after frontal lobe lesions in humans. *Cortex, 11*, 8-16.

Driver, J., & Spence, C. (2000). Multisensory perception: beyond modularity and convergence. *Curr Biol, 10*(20), R731-735.

Driver, J., & Noesselt, T. (2008). Multisensory interplay reveals crossmodal influences on 'sensory-specific' brain regions, neural responses, and judgments. *Neuron, 57*(1), 11-23.

Drullman, R., Festen, J. M., & Plomp, R. (1994). Effect of temporal envelope smearing on speech reception. *J Acoust Soc Am, 95*(2), 1053-1064.

Ecalle, J., Magnan, A., Bouchafa, H., & Gombert, J. E. (2009). Computer-based training with orthophonological units in dyslexic children: new investigations. *Dyslexia, 15*(3), 218-238.

Eden, G. F., Jones, K. M., Cappell, K., Gareau, L., Wood, F. B., Zeffiro, T. A., Dietz, N. A., Agnew, J. A., & Flowers, D. L. (2004). Neural changes following remediation in adult developmental dyslexia. *Neuron, 44*(3), 411-422.

Ehri, L. C., & Wilce, L. S. (1980). The influence orthography on readers conceptaualisation of the phonemic structure of words. *Applied Psycholinguistics, 1*, 371-385.

Ericsson, K. A., & Smith, J. (1991). *Prospects and limits of the empirical study of expertise: an introduction.* Cambridge: University Press.

Everatt, J., Jeffries, S., Elbeheri, G., Smythe, I., & Veii, K. (2006). Cross language learning disabilities and verbal versus spatial memory. *Cognitive Processing, 7*(7 (Supplement 1)).

Farah, M. J., Wong, A. B., Monheit, M. A., & Morrow, L. A. (1989). Parietal lobe mechanisms of spatial attention: modality-specific or supramodal? *Neuropsychologia, 27*(4), 461-470.

Farmer, M. E., & Klein, R. M. (1995). The evidence for a temporal preocessing deficit linked to dyslexia: a review. *Psychonomic Bulletin & Review, 2*, 460-493.

Fawcett, A. J., & Nicolson, R. I. (2007). Dyslexia, learning, and pedagogical neuroscience. *Dev Med Child Neurol, 49*(4), 306-311.

Fiez, J. A., & Petersen, S. E. (1998). Neuroimaging studies of word reading. *Proc Natl Acad Sci U S A, 95*(3), 914-921.

Forster, B., Cavina-Pratesi, C., Aglioti, S. M., & Berlucchi, G. (2002). Redundant target effect and intersensory facilitation from visual-tactile interactions in simple reaction time. *Exp Brain Res, 143*(4), 480-487.

Fox, P. T., & Raichle, M. E. (1986). Focal physiological uncoupling of cerebral blood flow and oxidative metabolism during somatosensory stimulation in human subjects. *Proc Natl Acad Sci U S A, 83*(4), 1140-1144.

Foxe, J. J., & Schroeder, C. E. (2005). The case for feedforward multisensory convergence during early cortical processing. *Neuroreport, 16*(5), 419-423.

Foxe, J. J. (2008). Toward the end of a "principled" era in multisensory science. *Brain Res, 1242*, 1-3.

Frackowiak, R. S., Friston, K. J., Frith, C. D., Dolan, R., Price, C. J., & Zeki, S. (2004). *Human Brain Function*. San Diego, CA: Academic Press/Elsevier Science.

France, S. J., Rosner, B. S., Hansen, P. C., Calvin, C., Talcott, J. B., Richardson, A. J., & Stein, J. F. (2002). Auditory frequency discrimination in adult developmental dyslexics. *Percept Psychophys, 64*(2), 169-179.

Fridlund, A. J. (1991). Sociality of Solitary Smiling: Potentiation by an Implicit Audience. *Journal of Personality and Social Psychology, 60*, 229-240.

Friston, K. J., Holmes, A. P., Worsley, K. J., Poline, J. P., Frith, C. D., & Frackowiak, R. S. J. (1995). Statistical parametric maps in functional imaging: a general linear approach. *Human Brain Mapping, 2*(189–210).

Frith, U. (1985). Beneath the surface of developmental Dyslexia Surface Dyslexia. In K. E. Patterson, J. C. Marshall & M. Coltheart (Eds.), *Neurophysiological and Cognitive Studies of Phonological Reading* (pp. 301-327). London: Erlbaum.

Frost, R. (1998). Toward a strong phonological theory of visual word recognition: true issues and false trails. *Psychol Bull, 123*(1), 71-99.

Fulbright, R. K., Jenner, A. R., Mencl, W. E., Pugh, K. R., Shaywitz, B. A., Shaywitz, S. E., Frost, S. J., Skudlarski, P., Constable, R. T., Lacadie, C. M., Marchione, K. E., & Gore, J. C. (1999). The cerebellum's role in reading: a functional MR imaging study. *AJNR Am J Neuroradiol, 20*(10), 1925-1930.

Gabrieli, J. D. (2009). Dyslexia: a new synergy between education and cognitive neuroscience. *Science, 325*(5938), 280-283.

Gaddum, J. H. (1945). Log-normal distributions. *Nature, 156*, 463-466.

Galaburda, A. M., LeMay, M., Kemper, T. L., & Geschwind, N. (1978). Right-left asymmetrics in the brain. *Science, 199*(4331), 852-856.

Galaburda, A. M., & Kemper, T. L. (1979). Cytoarchitectonic abnormalities in developmental dyslexia: a case study. *Ann Neurol, 6*(2), 94-100.

Galaburda, A. M. (1993). Neuroanatomic basis of developmental dyslexia. *Neurol Clin, 11*(1), 161-173.

Galaburda, A. M., Sherman, G. F., Rosen, G. D., Aboitiz, F., & Geschwind, N. (1985). Developmental dyslexia: four consecutive patients with cortical anomalies. *Ann Neurol, 18*(2), 222-233.

Galaburda, A. M., Menard, M. T., & Rosen, G. D. (1994). Evidence for aberrant auditory anatomy in developmental dyslexia. *Proc Natl Acad Sci U S A, 91*(17), 8010-8013.

Galaburda, A. M., LoTurco, J., Ramus, F., Fitch, R. H., & Rosen, G. D. (2006). From genes to behavior in developmental dyslexia. *Nat Neurosci, 9*(10), 1213-1217.

Gascon, G., & Goodglass, H. (1970). Reading retardation and the information content of stimuli in paired associate learning. *Cortex, 6*(4), 417-429.

Gathercole, S. E., Willis, C., & Baddeley, A. D. (1991). Differentiating phonological memory and awareness of rhyme: Reading and vocabulray development in children. *British Journal of Psychology, 82*(3), 387.

Gathercole, S. E., Pickering, S. J., Hall, M., & Peaker, S. M. (2001). Dissociable lexical and phonological influences on serial recognition and serial recall. *Q J Exp Psychol A, 54*(1), 1-30.

Gathercole, S. E., Alloway, T. P., Willis, C., & Adams, A.-M. (2006). Working memory in children with reading disabilities. *Journal of Experimental Child Psychology, 93*(3), 265-281.

Geiser, E., Zaehle, T., Jancke, L., & Meyer, M. (2008). The neural correlate of speech rhythm as evidenced by metrical speech processing. *J Cogn Neurosci, 20*(3), 541-552.

Georgiewa, P., Rzanny, R., Hopf, J. M., Knab, R., Glauche, V., Kaiser, W. A., & Blanz, B. (1999). fMRI during word processing in dyslexic and normal reading children. *Neuroreport, 10*(16), 3459-3465.

Georgiewa, P., Rzanny, R., Gaser, C., Gerhard, U.-J., Vieweg, U., Freesmeyer, D., Mentzel, H.-J., Kaiser, W. A., & Blanz, B. (2002). Phonological processing in dyslexic children: a study combining functional imaging and event related potentials. *Neuroscience Letters, 318*(1), 5-8.

Geschwind, N. (1965). Disconnexion syndromes in animals and man. II. *Brain, 88*(3), 585-644.

Geschwind, N., & Levitsky, W. (1968). Human brain: left-right asymmetries in temporal speech region. *Science, 161*(837), 186-187.

Ghazanfar, A. A., & Schroeder, C. E. (2006). Is neocortex essentially multisensory? *Trends Cogn Sci, 10*(6), 278-285.

Giard, M. H., & Peronnet, F. (1999). Auditory-Visual Integration during Multimodal Object Recognition in Humans: A Behavioral and Electrophysiological Study. *Journal of Cognitive Neuroscience, 11*(5), 473-490.

Goldberg, A. M., & Rapp, B. (2008). Is compound chaining the serial-order mechanism of spelling? A simple recurrent network investigation. *Cogn Neuropsychol, 25*(2), 218-255.

Goswami, U., Thomson, J., Richardson, U., Stainthorp, R., Hughes, D., Rosen, S., & Scott, S. K. (2002). Amplitude envelope onsets and developmental dyslexia: A new hypothesis. *Proc Natl Acad Sci U S A, 99*(16), 10911-10916.

Goswami, U., Ziegler, J. C., & Richardson, U. (2005). The effects of spelling consistency on phonological awareness: a comparison of English and German. *J Exp Child Psychol, 92*(4), 345-365.

Goswami, U. (2003). Why theories about developmental dyslexia require developmental designs. *Trends in Cognitive Sciences, 7*(12), 534-540.

Goswami, U., Wang, H.-L. S., Cruz, A., Fosker, T., Mead, N., & Huss, M. (2010). Language-universal Sensory Deficits in Developmental Dyslexia: English, Spanish, and Chinese. *Journal of Cognitive Neuroscience, 0*(0), 1-13.

Goyen, J. D., & Lyle, J. G. (1971). Effect of incentives upon retarded and normal readers on a visual-associated learning task. *J Exp Child Psychol, 11*(2), 274-280.

Grant, A. C., Zangaladze, A., Thiagarajah, M. C., & Sathian, K. (1999). Tactile perception in developmental dyslexia: a psychophysical study using gratings. *Neuropsychologia, 37*(10), 1201-1211.

Grigorenko, E. L., Wood, F. B., Meyer, M. S., Hart, L. A., Speed, W. C., Shuster, A., & Pauls, D. L. (1997). Susceptibility loci for distinct components of developmental dyslexia on chromosomes 6 and 15. *Am J Hum Genet, 60*(1), 27-39.

Gross, M., & Voegeli, C. (2007). A Multimedia Framework for Effective Language Training. *Computers & Graphics, 31*, 761-777.

Grossi, G., Coch, D., Coffey-Corina, S., Holcomb, P. J., & Neville, H. J. (2001). Phonological Processing in Visual Rhyming: A Developmental ERP Study. *Journal of Cognitive Neuroscience, 13*(5), 610-625.

Gross-Tsur, V., Shalev, R. S., Manor, O., & Amir, N. (1995). Developmental right-hemisphere syndrome: clinical spectrum of the nonverbal learning disability. *J Learn Disabil, 28*(2), 80-86.

Gross-Tsur, V., Manor, O., & Shalev, R. S. (1996). Developmental dyscalculia: prevalence and demographic features. *Dev Med Child Neurol, 38*(1), 25-33.

Grund, M., Haug, G., Naumann, C. L., & Weinheim, B.-V. (1995). *Diagnostischer Rechtschreibtest 5. Klasse*. Weinheim: Beltz-Verlag.

Habib, M. (2000). The neurological basis of developmental dyslexia: an overview and working hypothesis. *Brain, 123 Pt 12*, 2373-2399.

Hallgren, B. (1950). Specific dyslexia (congenital word-blindness); a clinical and genetic study. *Acta Psychiatr Neurol Suppl, 65*, 1-287.

Han, Z., & Bi, Y. (2009). Oral spelling and writing in a logographic language: Insights from a Chinese dysgraphic individual. *Brain and Language, 110*(1), 23-28.

Hannula-Jouppi, K., Kaminen-Ahola, N., Taipale, M., Eklund, R., Nopola-Hemmi, J., Kaariainen, H., & Kere, J. (2005). The axon guidance receptor gene ROBO1 is a candidate gene for developmental dyslexia. *PLoS Genet, 1*(4), e50.

Hari, R., & Renvall, H. (2001). Impaired processing of rapid stimulus sequences in dyslexia. *Trends Cogn Sci, 5*(12), 525-532.

Heathcote, A., Brown, S., & Mewhort, D. J. (2000). The power law repealed: the case for an exponential law of practice. *Psychonomic Bulletin & Review, 7*(2), 185-207.

Heiervang, E., Hugdahl, K., Steinmetz, H., Inge Smievoll, A., Stevenson, J., Lund, A., Ersland, L., & Lundervold, A. (2000). Planum temporale, planum parietale and dichotic listening in dyslexia. *Neuropsychologia, 38*(13), 1704-1713.

Hein, G., & Knight, R. T. (2008). Superior temporal sulcus--It's my area: or is it? *J Cogn Neurosci, 20*(12), 2125-2136.

Helenius, P., Tarkiainen, A., Cornelissen, P., Hansen, P. C., & Salmelin, R. (1999). Dissociation of normal feature analysis and deficient processing of letter-strings in dyslexic adults. *Cereb Cortex, 9*(5), 476-483.

Helland, T., & Asbjornsen, A. (2000). Executive functions in dyslexia. *Child Neuropsychol, 6*(1), 37-48.

Helland, T., & Asbjornsen, A. (2004). Digit span in dyslexia: variations according to language comprehension and mathematics skills. *J Clin Exp Neuropsychol, 26*(1), 31-42.

Henderson, L., & Chard, J. (1980). The reader's implicit knowledge of orthographic structure. In U. Frith (Ed.), *Cognitive processes in spelling* (pp. 85-116). New York: Academic Press.

Henderson, V. W. (1986). Anatomy of posterior pathways in reading: a reassessment. *Brain Lang, 29*(1), 119-133.

Hickok, G., & Poeppel, D. (2007). The cortical organization of speech processing. *Nat Rev Neurosci, 8*(5), 393-402.

Hickok, G. (2009). The functional neuroanatomy of language. *Phys Life Rev, 6*(3), 121-143.

Hill, G. T., & Raymond, J. E. (2002). Deficits of motion transparency perception in adult developmental dyslexics with normal unidirectional motion sensitivity. *Vision Research, 42*(9), 1195-1203.

Hilte, M., & Reitsma, P. (2006). Spelling pronunciation and visual preview both facilitate learning to spell irregular words. *Annals of Dyslexia, 56*(2), 301-318.

Hinojosa, J. A., Martín-Loeches, M., Muñoz, F., Casado, P., & Pozo, M. A. (2004). Electrophysiological evidence of automatic early semantic processing. *Brain and Language, 88*(1), 39-46.

Hu, W., Lee, H. L., Zhang, Q., Liu, T., Geng, L. B., Seghier, M. L., Shakeshaft, C., Twomey, T., Green, D. W., Yang, Y. M., & Price, C. J. (2010). Developmental dyslexia in Chinese and English populations: dissociating the effect of dyslexia from language differences. *Brain, 133*(6), 1694-1706.

Hulme, C., Goetz, K., Gooch, D., Adams, J., & Snowling, M. J. (2007). Paired-associate learning, phoneme awareness, and learning to read. *J Exp Child Psychol, 96*(2), 150-166.

Humphreys, P., Kaufmann, W. E., & Galaburda, A. M. (1990). Developmental dyslexia in women: neuropathological findings in three patients. *Ann Neurol, 28*(6), 727-738.

Huss, M., Verney, J. P., Fosker, T., Mead, N., & Goswami, U. (2010). Music, rhythm, rise time perception and developmental dyslexia: Perception of musical meter predicts reading and phonology. *Cortex, In Press, Corrected Proof*.

Ito, M. (1984). The modifiable neuronal network of the cerebellum. *Jpn J Physiol, 34*(5), 781-792.

Ito, M. (1993). Movement and thought: identical control mechanisms by the cerebellum. *Trends Neurosci, 16*(11), 448-450; discussion 453-444.

Jasper, H. (1958). The ten-twenty system of the international federation. *Electroencephalogr Clin Neurophysiol, 10*, 371-375.

Jobard, G., Crivello, F., & Tzourio-Mazoyer, N. (2003). Evaluation of the dual route theory of reading: a metanalysis of 35 neuroimaging studies. *Neuroimage, 20*(2), 693-712.

Johannes, S., Kussmaul, C. L., Munte, T. F., & Mangun, G. R. (1996). Developmental dyslexia: passive visual stimulation provides no evidence for a magnocellular processing defect. *Neuropsychologia, 34*(11), 1123-1127.

Jorm, A. F. (1983). Specific reading retardation and working memory: a review. *Br J Psychol, 74 (3)*, 311-342.

Jung, T.-P., Makeig, S., Humphries, C., Lee, T.-W., McKeown, M. J., Iragui, V., & Sejnowski, T. J. (2000). Removing electroencephalographic artifacts by blind source separation. *Psychophysiology, 37*(2), 163-178.

Kast, M., Meyer, M., Vogeli, C., Gross, M., & Jancke, L. (2007). Computer-based multisensory learning in children with developmental dyslexia. *Restorative Neurology and Neuroscience, 25*(3-4), 355-369.

Kast, M., Elmer, S., Jancke, L., & Meyer, M. (2010). ERP differences of pre-lexical processing between dyslexic and non-dyslexic children. *Int J Psychophysiol*.

Kaufmann, W. E., & Galaburda, A. M. (1989). Cerebrocortical microdysgenesis in neurologically normal subjects: a histopathologic study. *Neurology, 39*(2 Pt 1), 238-244.

Keller, T. A., Carpenter, P. A., & Just, M. A. (2001). The neural bases of sentence comprehension: a fMRI examination of syntactic and lexical processing. *Cereb Cortex, 11*(3), 223-237.

Kersting, M., & Althoff, K. (2004). *RT Rechtschreibungstest.* Göttingen: Hogrefe Verlag für Psychologie.

Kita, Y., Mori, A., & Nara, M. (2001). Two types of movement-related cortical potentials preceding wrist extension in humans. *Neuroreport, 12*(10), 2221-2225.

Klingberg, T., Hedehus, M., Temple, E., Salz, T., Gabrieli, J. D., Moseley, M. E., & Poldrack, R. A. (2000). Microstructure of temporo-parietal white matter as a basis for reading ability: evidence from diffusion tensor magnetic resonance imaging. *Neuron, 25*(2), 493-500.

Kötter, R. (2008). Funktionelle neuroanatomie der Inselrinde (functional neuroanatomy of the insular cortex). *Nervenheilkunde, 27*, 425-429.

Kronbichler, M., Hutzler, F., & Wimmer, H. (2002). Dyslexia: verbal impairments in the absence of magnocellular impairments. *Neuroreport, 13*(5), 617-620.

Kujala, T., Myllyviita, K., Tervaniemi, M., Alho, K., Kallio, J., & Naatanen, R. (2000). Basic auditory dysfunction in dyslexia as demonstrated by brain activity measurements. *Psychophysiology, 37*(2), 262-266.

Kujala, T., Karma, K., Ceponiene, R., Belitz, S., Turkkila, P., Tervaniemi, M., & Naatanen, R. (2001). Plastic neural changes and reading improvement caused by audiovisual training in reading-impaired children. *Proc Natl Acad Sci U S A, 98*(18), 10509-10514.

Kushch, A., Gross-Glenn, K., Jallad, B., Lubs, H., Rabin, M., Feldman, E., & Duara, R. (1993). Temporal lobe surface area measurements on MRI in normal and dyslexic readers. *Neuropsychologia, 31*(8), 811-821.

Kutas, M., & Hillyard, S. A. (1980). Reading senseless sentences: brain potentials reflect semantic incongruity. *Science, 207*(4427), 203-205.

Kutas, M., & Federmeier, K. D. (2000). Electrophysiology reveals semantic memory use in language comprehension. *Trends Cogn Sci, 4*(12), 463-470.

Landerl, K., Wimmer, H., & Frith, U. (1997). The impact of orthographic consistency on dyslexia: a German-English comparison. *Cognition, 63*(3), 315-334.

Larsen, J. P., Hoien, T., Lundberg, I., & Odegaard, H. (1990). MRI evaluation of the size and symmetry of the planum temporale in adolescents with developmental dyslexia. *Brain Lang, 39*(2), 289-301.

Lashley, K. S. (1951). The problem of serial order in behavior. In F. Beach, D. Hebb, C. Morgan & H. Nissen (Eds.), *The Neuropsychology of Lashley 1960* (pp. 506-528). New York: McGraw-Hill.

Lawler, A. (2001). Archaeology. Writing gets a rewrite. *Science, 292*(5526), 2418-2420.

Lehmann, S., & Murray, M. M. (2005). The role of multisensory memories in unisensory object discrimination. *Brain Res Cogn Brain Res, 24*(2), 326-334.

Leiner, H. C., Leiner, A. L., & Dow, R. S. (1989). Reappraising the cerebellum: what does the hindbrain contribute to the forebrain? *Behav Neurosci, 103*(5), 998-1008.

Leiner, H. C., Leiner, A. L., & Dow, R. S. (1993). Cognitive and language functions of the human cerebellum. *Trends Neurosci, 16*(11), 444-447.

Lerner, J. W. (1989). Educational interventions in learning disabilities. *J Am Acad Child Adolesc Psychiatry, 28*(3), 326-331.

Lewis, J. W., Beauchamp, M. S., & DeYoe, E. A. (2000). A comparison of visual and auditory motion processing in human cerebral cortex. *Cereb Cortex, 10*(9), 873-888.

Lezak, M. (1995). *Neuropschological Assessment*. New York: Oxford University Press.

Li, H., Shu, H., McBride-Chang, C., Liu, H. Y., & Xue, J. (2009). Paired associate learning in Chinese children with dyslexia. *J Exp Child Psychol, 103*(2), 135-151.

Liberman, I. Y., Shankweiler, D., Fischer, F. W., & Carter, B. (1974). Explicit syllable and phoneme segmentation in the young child. *Journal of Experimental Child Psychology, 18*(2), 201-212.

Liberman, A. M. (1998). Why is speech so much easier than reading and writing. In C. Hulme & R. M. Malate-sha (Eds.), *Reading and spelling: development and disorders* (pp. 5-17). Mahwah, NJ: Lawrence Erlbaum.

Lim, K. O., & Helpern, J. A. (2002). Neuropsychiatric applications of DTI - a review. *NMR Biomed, 15*(7-8), 587-593.

Linder, M., & Grissemann, H. (2000). *Zürcher Lesetest*. Bern-Göttingen: Hogrefe-Verlag.

Livingstone, M., & Hubel, D. (1988). Segregation of form, color, movement, and depth: anatomy, physiology, and perception. *Science, 240*(4853), 740-749.

Livingstone, M. S., Rosen, G. D., Drislane, F. W., & Galaburda, A. M. (1991). Physiological and anatomical evidence for a magnocellular defect in developmental dyslexia. *Proc Natl Acad Sci U S A, 88*(18), 7943-7947.

Logan, G. D. (1988). Toward an instance theory of automatization. *Psychological, 95*, 492-527.

Lovegrove, W. J., Bowling, A., Badcock, D., & Blackwood, M. (1980). Specific reading disability: differences in contrast sensitivity as a function of spatial frequency. *Science, 210*(4468), 439-440.

Lux, S., Helmstaedter, C., & Elger, C. E. (1999). *Normative study on the "Verbaler Lern- und Merkfahigkeitstest" (VLMT)*: Diagnostica.

Lyon, G. R. (1995). Toward a definition of dyslexia. *Annals of Dyslexia, 45*, 3-27.

Lyon, G., Shaywitz, S., & Shaywitz, B. (2003). A definition of dyslexia, *Annals of Dyslexia* (53, 1-14).

Maisog, J. M., Einbinder, E. R., Flowers, D. L., Turkeltaub, P. E., & Eden, G. F. (2008). A Meta-analysis of Functional Neuroimaging Studies of Dyslexia. *Annals of the New York Academy of Sciences, 1145*(Learning, Skill Acquisition, Reading, and Dyslexia), 237-259.

Manis, F. R., Custodio, R., & Szeszulski, P. A. (1993). Development of Phonological and Orthographic Skill: A 2-Year Longitudinal Study of Dyslexic Children. *Journal of Experimental Child Psychology, 56*(1), 64-86.

Manis, F. R., McBride-Chang, C., Seidenberg, M. S., Keating, P., Doi, L. M., Munson, B., & Petersen, A. (1997). Are speech perception deficits associated with developmental dyslexia? *J Exp Child Psychol, 66*(2), 211-235.

Manis, F. R., Doi, L. M., & Bhadha, B. (2000). Naming speed, phonological awareness, and orthographic knowledge in second graders. *J Learn Disabil, 33*(4), 325-333, 374.

Mann, V. A., Liberman, I. Y., & Shankweiler, D. (1980). Children's memory for sentences and word strings in relation to reading ability. *Mem Cognit, 8*(4), 329-335.

Marshall, C. M., Snowling, M. J., & Bailey, P. J. (2001). Rapid auditory processing and phonological ability in normal readers and readers with dyslexia. *J Speech Lang Hear Res, 44*(4), 925-940.

Martin, F., & Lovegrove, W. (1987). Flicker contrast sensitivity in normal and specifically disabled readers. *Perception, 16*(2), 215-221.

Martin-Loeches, M., Hinojosa, J. A., Gomez-Jarabo, G., & Rubia, F. J. (1999). The recognition potential : an ERP index of lexical access. *Brain & Language, 70*, 364-384.

Mathias, J. L., Bigler, E. D., Jones, N. R., Bowden, S. C., Barrett-Woodbridge, M., Brown, G. C., & Taylor, D. J. (2004). Neuropsychological and information processing performance and its relationship to white matter changes following moderate and severe traumatic brain injury: a preliminary study. *Appl Neuropsychol, 11*(3), 134-152.

Maurer, U., Brem, S., Bucher, K., & Brandeis, D. (2005). Emerging neurophysiological specialization for letter strings. *J Cogn Neurosci, 17*(10), 1532-1552.

Maurer, U., Brem, S., Kranz, F., Bucher, K., Benz, R., Halder, P., Steinhausen, H. C., & Brandeis, D. (2006). Coarse neural tuning for print peaks when children learn to read. *Neuroimage, 33*(2), 749-758.

Maurer, U., Brem, S., Bucher, K., Kranz, F., Benz, R., Steinhausen, H. C., & Brandeis, D. (2007). Impaired tuning of a fast occipito-temporal response for print in dyslexic children learning to read. *Brain, 130*(Pt 12), 3200-3210.

Maurer, U., Rossion, B., & McCandliss, B. D. (2008a). Category specificity in early perception: face and word N170 responses differ in both lateralization and habituation properties. *Frontiers in human neuroscience, 2*(1-7).

Maurer, U., Zevin, J. D., & McCandliss, B. D. (2008b). Left-lateralized N170 effects of visual expertise in reading: evidence from Japanese syllabic and logographic scripts. *J Cogn Neurosci, 20*(10), 1878-1891.

McCandliss, B. D., Cohen, L., & Dehaene, S. (2003a). The visual word form area: expertise for reading in the fusiform gyrus. *Trends Cogn Sci, 7*(7), 293-299.

McCandliss, B. D., & Noble, K. G. (2003b). The development of reading impairment: a cognitive neuroscience model. *Ment Retard Dev Disabil Res Rev, 9*(3), 196-204.

Menghini, D., Hagberg, G. E., Petrosini, L., Bozzali, M., Macaluso, E., Caltagirone, C., & Vicari, S. (2008). Structural correlates of implicit learning deficits in subjects with developmental dyslexia. *Ann N Y Acad Sci, 1145*, 212-221.

Menon, V., & Uddin, L. Q. (2010). Saliency, switching, attention and control: a network model of insula function. *Brain Struct Funct, 214*(5-6), 655-667.

Meredith, M. A., & Stein, B. E. (1983). Interactions among converging sensory inputs in the superior colliculus. *Science, 221*(4608), 389-391.

Messbauer, V. C., & de Jong, P. F. (2003). Word, nonword, and visual paired associate learning in Dutch dyslexic children. *J Exp Child Psychol, 84*(2), 77-96.

Meyer, M., Friederici, A. D., & von Cramon, D. Y. (2000). Neurocognition of auditory sentence comprehension: event related fMRI reveals sensitivity to syntactic violations and task demands. *Brain Res Cogn Brain Res, 9*(1), 19-33.

Meyer, M., Alter, K., Friederici, A. D., Lohmann, G., & von Cramon, D. Y. (2002). FMRI reveals brain regions mediating slow prosodic modulations in spoken sentences. *Hum Brain Mapp, 17*(2), 73-88.

Meyer, M., Alter, K., & Friederici, A. (2003). Functional MR imaging exposes differential brain responses to syntax and prosody during auditory sentence comprehension. *Journal of Neurolinguistics, 16*(4-5), 277-300.

Meyer, M., Baumann, S., & Jancke, L. (2006). Electrical brain imaging reveals spatio-temporal dynamics of timbre perception in humans. *Neuroimage, 32*(4), 1510-1523.

Meyer, M., Elmer, S., Baumann, S., & Jancke, L. (2007). Short-term plasticity in the auditory system: differential neural responses to perception and imagery of speech and music. *Restor Neurol Neurosci, 25*(3-4), 411-431.

Meyler, A., Keller, T. A., Cherkassky, V. L., Lee, D., Hoeft, F., Whitfield-Gabrieli, S., Gabrieli, J. D., & Just, M. A. (2007). Brain activation during sentence comprehension among good and poor readers. *Cereb Cortex, 17*(12), 2780-2787.

Meyler, A., Keller, T. A., Cherkassky, V. L., Gabrieli, J. D., & Just, M. A. (2008). Modifying the brain activation of poor readers during sentence comprehension with extended remedial instruction: a longitudinal study of neuroplasticity. *Neuropsychologia, 46*(10), 2580-2592.

Micheloyannis, S., Pachou, E., Stam, C. J., Vourkas, M., Erimaki, S., & Tsirka, V. (2006). Using graph theoretical analysis of multi channel EEG to evaluate the neural efficiency hypothesis. *Neurosci Lett, 402*(3), 273-277.

Middleton, F. A., & Strick, P. L. (1997). Cerebellar output channels. *Int Rev Neurobiol, 41*, 61-82.

Miller, L. M., & D'Esposito, M. (2005). Perceptual fusion and stimulus coincidence in the cross-modal integration of speech. *J Neurosci, 25*(25), 5884-5893.

Miller, P., & Kupfermann, A. (2009). The role of visual and phonological representations in the processing of written words by readers with diagnosed dyslexia: evidence from a working memory task. *Annals of Dyslexia, 59*(1), 12-33.

Molholm, S., Ritter, W., Murray, M. M., Javitt, D. C., Schroeder, C. E., & Foxe, J. J. (2002). Multisensory auditory-visual interactions during early sensory processing in humans: a high-density electrical mapping study. *Cognitive Brain Research, 14*(1), 115-128.

Molholm, S., Ritter, W., Javitt, D. C., & Foxe, J. J. (2004). Multisensory visual-auditory object recognition in humans: a high-density electrical mapping study. *Cereb Cortex, 14*(4), 452-465.

Molholm, S., Sehatpour, P., Mehta, A. D., Shpaner, M., Gomez-Ramirez, M., Ortigue, S., Dyke, J. P., Schwartz, T. H., & Foxe, J. J. (2006). Audio-visual multisensory integration in superior parietal lobule revealed by human intracranial recordings. *J Neurophysiol, 96*(2), 721-729.

Moran, R. J., Molholm, S., Reilly, R. B., & Foxe, J. J. (2008). Changes in effective connectivity of human superior parietal lobule under multisensory and unisensory stimulation. *Eur J Neurosci, 27*(9), 2303-2312.

Mukherjee, P., Bahn, M. M., McKinstry, R. C., Shimony, J. S., Cull, T. S., Akbudak, E., Snyder, A. Z., & Conturo, T. E. (2000). Differences between gray matter and white matter water diffusion in stroke: diffusion-tensor MR imaging in 12 patients. *Radiology, 215*(1), 211-220.

Murray, M. M., Michel, C. M., Grave de Peralta, R., Ortigue, S., Brunet, D., Gonzalez Andino, S., & Schnider, A. (2004). Rapid discrimination of visual and multisensory memories revealed by electrical neuroimaging. *Neuroimage, 21*(1), 125-135.

Muter, V., Hulme, C., Snowling, M. J., & Stevenson, J. (2004). Phonemes, rimes, vocabulary, and grammatical skills as foundations of early reading development: evidence from a longitudinal study. *Dev Psychol, 40*(5), 665-681.

Mutschler, I., Wieckhorst, B., Kowalevski, S., Derix, J., Wentlandt, J., Schulze-Bonhage, A., & Ball, T. (2009). Functional organization of the human anterior insular cortex. *Neurosci Lett, 457*(2), 66-70.

Nadeau, S. E. (1988). Impaired grammar with normal fluency and phonology. Implications for Broca's aphasia. *Brain, 111 (Pt 5)*, 1111-1137.

Nagy, Z., Westerberg, H., & Klingberg, T. (2004). Maturation of white matter is associated with the development of cognitive functions during childhood. *J Cogn Neurosci, 16*(7), 1227-1233.

Newell, A., & Rosenbloom, P. S. (1981). Mechanismus of Skill Acqusition and the Law of Pracitce. In J. R. Anderson (Ed.), *Cognitive Skills and their acquistion* (pp. 1-55). Hillsdale, NJ: Lawrence Erlbaum Associates.

Nicolson, R. I., & Fawcett, A. J. (1990). Automaticity: a new framework for dyslexia research? *Cognition, 35*(2), 159-182.

Nicolson, R. I., & Fawcett, A. J. (1994). Reaction times and dyslexia. *Q J Exp Psychol A, 47*(1), 29-48.

Nicolson, R. I., Fawcett, A. J., & Dean, P. (1995). Time estimation deficits in developmental dyslexia: evidence of cerebellar involvement. *Proc Biol Sci, 259*(1354), 43-47.

Nicolson, R. I., Fawcett, A. J., Berry, E. L., Jenkins, I. H., Dean, P., & Brooks, D. J. (1999). Association of abnormal cerebellar activation with motor learning difficulties in dyslexic adults. *Lancet, 353*(9165), 1662-1667.

Niogi, S. N., & McCandliss, B. D. (2006). Left lateralized white matter microstructure accounts for individual differences in reading ability and disability. *Neuropsychologia, 44*(11), 2178-2188.

Nobre, A. C., Allison, T., & McCarthy, G. (1994). Word recognition in the human inferior temporal lobe. *Nature, 372*(6503), 260-263.

Nyberg, L., Habib, R., McIntosh, A. R., & Tulving, E. (2000). Reactivation of encoding-related brain activity during memory retrieval. *Proc Natl Acad Sci U S A, 97*(20), 11120-11124.

Ogawa, S., Lee, T. M., Nayak, A. S., & Glynn, P. (1990). Oxygenation-sensitive contrast in magnetic resonance image of rodent brain at high magnetic fields. *Magn Reson Med, 14*(1), 68-78.

Ojemann, G., Ojemann, J., Lettich, E., & Berger, M. (1989). Cortical language localization in left, dominant hemisphere. An electrical stimulation mapping investigation in 117 patients. *J Neurosurg, 71*(3), 316-326.

Olesen, P. J., Nagy, Z., Westerberg, H., & Klingberg, T. (2003). Combined analysis of DTI and fMRI data reveals a joint maturation of white and grey matter in a fronto-parietal network. *Brain Res Cogn Brain Res, 18*(1), 48-57.

Olson, R., Wise, B., Conners, F., Rack, J., & Fulker, D. (1989). Specific deficits in component reading and language skills: genetic and environmental influences. *J Learn Disabil, 22*(6), 339-348.

Pammer, K., Hansen, P. C., Kringelbach, M. L., Holliday, I., Barnes, G., Hillebrand, A., Singh, K. D., & Cornelissen, P. L. (2004). Visual word recognition: the first half second. *Neuroimage, 22*(4), 1819-1825.

Pammer, K., & Vidyasagar, T. R. (2005). Integration of the visual and auditory networks in dyslexia: a theoretical perspective. *Journal of Research in Reading, 28*(3), 320-331.

Pascual-Marqui, R. D., Michel, C. M., & Lehmann, D. (1994). Low resolution electromagnetic tomography: a new method for localizing electrical activity in the brain. *Int J Psychophysiol, 18*(1), 49-65.

Pascual-Marqui, R. D. (2002). Standardized low resolution brain electromagnetic tomography (sLORETA): technical details. *Experimental & Clinical Pharmacology, 24*, 5-12.

Paulesu, E., Frith, U., Snowling, M., Gallagher, A., Morton, J., Frackowiak, R. S., & Frith, C. D. (1996). Is developmental dyslexia a disconnection syndrome? Evidence from PET scanning. *Brain, 119 (1)*, 143-157.

Paulesu, E., Demonet, J. F., Fazio, F., McCrory, E., Chanoine, V., Brunswick, N., Cappa, S. F., Cossu, G., Habib, M., Frith, C. D., & Frith, U. (2001). Dyslexia: cultural diversity and biological unity. *Science, 291*(5511), 2165-2167.

Peereman, R., Dufour, S., & Burt, J. S. (2009). Orthographic influences in spoken word recognition: the consistency effect in semantic and gender categorization tasks. *Psychon Bull Rev, 16*(2), 363-368.

Plaut, D. C., McClelland, J. L., Seidenberg, M. S., & Patterson, K. (1996). Understanding normal and impaired word reading: computational principles in quasi-regular domains. *Psychol Rev, 103*(1), 56-115.

Poelmans, G., Engelen, J. J., Van Lent-Albrechts, J., Smeets, H. J., Schoenmakers, E., Franke, B., Buitelaar, J. K., Wuisman-Frerker, M., Erens, W., Steyaert, J., & Schrander-Stumpel, C. (2009). Identification of novel dyslexia candidate genes through the analysis of a chromosomal deletion. *Am J Med Genet B Neuropsychiatr Genet, 150B*(1), 140-147.

Poeppel, D. (2003). The analysis of speech in different temporal integration windows: cerebral lateralization as asymmetric sampling in time. *Speech Communication, 41*(1), 245-255.

Polk, T. A., Stallcup, M., Aguirre, G. K., Alsop, D. C., D'Esposito, M., Detre, J. A., & Farah, M. J. (2002). Neural specialization for letter recognition. *J Cogn Neurosci, 14*(2), 145-159.

Posner, M. I., & Presti, D. (1987). Selective attention and cognitive control. *Trends in Neuroscience, 10*, 12-17.

Posner, M. I., & Rafal, R. D. (1987). Cognitive theories of attention and the rehabilitation of attentional deficits. In R. J. Meier, A. C. Benton & L. Diller (Eds.), *Neuropsychological Rehabilitation*. Edinburgh: Churchill Livingstone.

Pourtois, G., & de Gelder, B. (2002). Semantic factors influence multisensory pairing: a transcranial magnetic stimulation study. *Neuroreport, 13*(12), 1567-1573.

Price, C. J. (2000). The anatomy of language: contributions from functional neuroimaging. *J Anat, 197 Pt 3*, 335-359.

Price, C. J., Warburton, E. A., Moore, C. J., Frackowiak, R. S. J., & Friston, K. J. (2001). Dynamic diaschisis: anatomically remote and context-sensitive human brain lesions. *Journal of Cognitive Neuroscience, 13*(4), 419-429.

Pruessmann, K. P., Weiger, M., Scheidegger, M. B., & Boesiger, P. (1999). SENSE: Sensitivity encoding for fast MRI. *Magnetic Resonance in Medicine, 42*(5), 952-962.

Puce, A., Allison, T., & McCarthy, G. (1999). Electrophysiological Studies of Human Face Perception. III: Effects of Top-down Processing on Face-specific Potentials. *Cerebral Cortex 9* (5), 445-458

Pugh, K. R., Mencl, W. E., Jenner, A. R., Katz, L., Frost, S. J., Lee, J. R., Shaywitz, S. E., & Shaywitz, B. A. (2000a). Functional neuroimaging studies of reading and reading disability (developmental dyslexia). *Ment Retard Dev Disabil Res Rev, 6*(3), 207-213.

Pugh, K. R., Mencl, W. E., Shaywitz, B. A., Shaywitz, S. E., Fulbright, R. K., Constable, R. T., Skudlarski, P., Marchione, K. E., Jenner, A. R., Fletcher, J. M., Liberman, A. M., Shankweiler, D. P., Katz, L., Lacadie, C., & Gore, J. C. (2000b). The angular gyrus in developmental dyslexia: task-specific differences in functional connectivity within posterior cortex. *Psychol Sci, 11*(1), 51-56.

Raij, T., Uutela, K., & Hari, R. (2000). Audiovisual integration of letters in the human brain. *Neuron, 28*(2), 617-625.

Ramus, F. (2001). Dyslexia. Talk of two theories. *Nature, 412*(6845), 393-395.

Ramus, F. (2003). Developmental dyslexia: specific phonological deficit or general sensorimotor dysfunction? *Curr Opin Neurobiol, 13*(2), 212-218.

Ramus, F., Pidgeon, E., & Frith, U. (2003a). The relationship between motor control and phonology in dyslexic children. *Journal of Child Psychology and Psychiatry, 44*(5), 712-722.

Ramus, F., Rosen, S., Dakin, S. C., Day, B. L., Castellote, J. M., White, S., & Frith, U. (2003b). Theories of developmental dyslexia: insights from a multiple case study of dyslexic adults. *Brain, 126*(Pt 4), 841-865.

Ramus, F., Rosen, S., Dakin, S. C., Day, B. L., Castellote, J. M., White, S., & Frith, U. (2003c). Theories of developmental dyslexia: insights from a multiple case study of dyslexic adults. *Brain, 126*(4), 841-865.

Ramus, F. (2004). Neurobiology of dyslexia: a reinterpretation of the data. *Trends Neurosci, 27*(12), 720-726.

Rapin, I., & Allen, D. A. (1988). Syndromes in developmental dysphasia and adult aphasia. *Res Publ Assoc Res Nerv Ment Dis, 66*, 57-75.

Rapp, B., & Caramazza, A. (1997). From graphemes to abstract letter shapes: levels of representation in written spelling. *J Exp Psychol Hum Percept Perform, 23*(4), 1130-1152.

Rastle, K., & Brysbaert, M. (2006). Masked phonological priming effects in English: are they real? Do they matter? *Cogn Psychol, 53*(2), 97-145.

Re, A. M., Caeran, M., & Cornoldi, C. (2008). Improving Expressive Writing Skills of Children Rated for ADHD Symptoms. *Journal of Learning Disabilities, 41*(6), 535-544.

Reed, M. A. (1989). Speech perception and the discrimination of brief auditory cues in reading disabled children. *J Exp Child Psychol, 48*(2), 270-292.

Reicher, G. M. (1969). Perceptual recognition as a function of meaningfulness of stimulus material. *Journal of Experimental Psychology, 81*, 274-280.

Reiter, A., Tucha, O., & Lange, K. W. (2005). Executive functions in children with dyslexia. *Dyslexia, 11*(2), 116-131.

Rey, V., De Martino, S., Espesser, R., & Habib, M. (2002). Temporal processing and phonological impairment in dyslexia: effect of phoneme lengthening on order judgment of two consonants. *Brain Lang, 80*(3), 576-591.

Richards, T., Berninger, V., Winn, W., Stock, P., Wagner, R., Muse, A., & Maravilla, K. (2007). Functional MRI activation in children with and without dyslexia during pseudoword aural repeat and visual decode: before and after treatment. *Neuropsychology, 21*(6), 732-741.

Robichon, F., & Habib, M. (1998). Abnormal callosal morphology in male adult dyslexics: relationships to handedness and phonological abilities. *Brain Lang, 62*(1), 127-146.

Rosen, S., & Manganari, E. (2001). Is there a relationship between speech and nonspeech auditory processing in children with dyslexia? *J Speech Lang Hear Res, 44*(4), 720-736.

Rosen, S. (2003). Auditory processing in dyslexia and specific language impairment: Is there a deficit? What is its nature? Does it explain anything? *J. Phonetics, 31*, 509-527.

Rossion, B., Joyce, C. A., Cottrell, G. W., & Tarr, M. J. (2003). Early lateralization and orientation tuning for face, word, and object processing in the visual cortex. *Neuroimage, 20*(3), 1609-1624.

Rudel, R. G. (1985). The definition of dyslexia: language and motor deficits. In F. H. Duffy & H. Gschwind (Eds.), *Dyslexia: a neuroscientific approach to clinical evaluation* (pp. 33-53). Boston: Little Brown.

Rudell, A. P. (1991). The Recognition Potential Contrasted with the P300. *International Journal of Neuroscience, 60*, 85-111.

Rumsey, J. M., Andreason, P., Zametkin, A. J., Aquino, T., King, A. C., Hamburger, S. D., Pikus, A., Rapoport, J. L., & Cohen, R. M. (1992). Failure to activate the left temporoparietal cortex in dyslexia. An oxygen 15 positron emission tomographic study. *Arch Neurol, 49*(5), 527-534.

Rumsey, J. M., Donohue, B. C., Brady, D. R., Nace, K., Giedd, J. N., & Andreason, P. (1997a). A magnetic resonance imaging study of planum temporale asymmetry in men with developmental dyslexia. *Arch Neurol, 54*(12), 1481-1489.

Rumsey, J. M., Horwitz, B., Donohue, B. C., Nace, K., Maisog, J. M., & Andreason, P. (1997b). Phonological and orthographic components of word recognition. A PET-rCBF study. *Brain, 120 (5)*, 739-759.

Rumsey, J. M., Horwitz, B., Donohue, B. C., Nace, K. L., Maisog, J. M., & Andreason, P. (1999). A functional lesion in developmental dyslexia: left angular gyral blood flow predicts severity. *Brain Lang, 70*(2), 187-204.

Russeler, J., Probst, S., Johannes, S., & Munte, T. (2003). Recognition memory for high- and low-frequency words in adult normal and dyslexic readers: an event-related brain potential study. *J Clin Exp Neuropsychol, 25*(6), 815-829.

Russeler, J. (2006). Neurobiologische Grundlagen der Lese-Rechtschreib-Schwäche Implikationen für Diagnostik und Therapie. *Zeitschrift für Neuropsychologie, 17*(2), 101–111.

Russeler, J., Gerth, I., & Munte, T. F. (2006). Implicit learning is intact in adult developmental dyslexic readers: evidence from the serial reaction time task and artificial grammar learning. *J Clin Exp Neuropsychol, 28*(5), 808-827.

Salmelin, R., Helenius, P., & Service, E. (2000). Neurophysiology of Fluent and Impaired Reading: A Magnetoencephalographic Approach. *Journal of Clinical Neurophysiology, 17*(163-174).

Salmelin, R., & Helenius, P. (2004). Functional Neuroanatomy of Impaired Reading in Dyslexia. *Scientific Studies of Reading, 8*(3), 257-272.

Salmelin, R., & Kujala, J. (2006). Neural representation of language: activation versus long-range connectivity. *Trends in Cognitive Sciences, 10*(11), 519-525.

Sandak, R., Mencl, W. E., Frost, S. J., Rueckl, J. G., Katz, L., Moore, D. L., Mason, S. A., Fulbright, R. K., Constable, R. T., & Pugh, K. R. (2004). The neurobiology of adaptive learning in reading: a contrast of different training conditions. *Cogn Affect Behav Neurosci, 4*(1), 67-88.

Saur, D., Kreher, B. W., Schnell, S., Kummerer, D., Kellmeyer, P., Vry, M. S., Umarova, R., Musso, M., Glauche, V., Abel, S., Huber, W., Rijntjes, M., Hennig, J., & Weiller, C. (2008). Ventral and dorsal pathways for language. *Proc Natl Acad Sci U S A, 105*(46), 18035-18040.

Savage, R. S., & Frederickson, N. (2006). Beyond phonology: What else is needed to describe the problems of below-average readers and spellers? *J Learn Disabil, 39*(5), 399-413.

Schmahmann, J. D., & Pandya, D. N. (1997). The cerebrocerebellar system. *Int Rev Neurobiol, 41*, 31-60.

Schroeder, C. E., & Foxe, J. J. (2002). The timing and laminar profile of converging inputs to multisensory areas of the macaque neocortex. *Brain Res Cogn Brain Res, 14*(1), 187-198.

Schulte-Korne, G., Bartling, J., Deimel, W., & Remschmidt, H. (2004a). Spatial-frequency- and contrast-dependent visible persistence and reading disorder: no evidence for a basic perceptual deficit. *Journal of Neural Transmission, 111*(7), 941-950.

Schulte-Korne, G., Deimel, W., Bartling, J., & Remschmidt, H. (2004b). Neurophysiological correlates of word recognition in dyslexia. *J Neural Transm, 111*(7), 971-984.

Seidenberg, M. S., & McClelland, J. L. (1989). A distributed, developmental model of word recognition and naming. *Psychol Rev, 96*(4), 523-568.

Sekiyama, K., Kanno, I., Miura, S., & Sugita, Y. (2003). Auditory-visual speech perception examined by fMRI and PET. *Neurosci Res, 47*(3), 277-287.

Seltzer, B., & Pandya, D. N. (1980). Converging visual and somatic sensory cortical input to the intraparietal sulcus of the rhesus monkey. *Brain Res, 192*(2), 339-351.

Seltzer, B., & Pandya, D. N. (1994). Parietal, temporal, and occipital projections to cortex of the superior temporal sulcus in the rhesus monkey: a retrograde tracer study. *J Comp Neurol, 343*(3), 445-463.

Serniclaes, W., Sprenger-Charolles, L., Carre, R., & Demonet, J. F. (2001). Perceptual discrimination of speech sounds in developmental dyslexia. *J Speech Lang Hear Res, 44*(2), 384-399.

Shallice, T. (1981). Phonological agraphia and the lexical route in writing. *Brain, 104*(3), 413-429.

Shams, L., & Seitz, A. R. (2008). Benefits of multisensory learning. *Trends Cogn Sci, 12*(11), 411-417.

Shapleske, J., Rossell, S. L., Woodruff, P. W., & David, A. S. (1999). The planum temporale: a systematic, quantitative review of its structural, functional and clinical significance. *Brain Res Brain Res Rev, 29*(1), 26-49.

Shaywitz, S. E. (1998). Dyslexia. *N Engl J Med, 338*(5), 307-312.

Shaywitz, S. E., Shaywitz, B. A., Pugh, K. R., Fulbright, R. K., Constable, R. T., Mencl, W. E., Shankweiler, D. P., Liberman, A. M., Skudlarski, P., Fletcher, J. M., Katz, L., Marchione, K. E., Lacadie, C., Gatenby, C., & Gore, J. C. (1998). Functional disruption in the organization of the brain for reading in dyslexia. *Proc Natl Acad Sci U S A, 95*(5), 2636-2641.

Shaywitz, B. A., Shaywitz, S. E., Pugh, K. R., Mencl, W. E., Fulbright, R. K., Skudlarski, P., Constable, R. T., Marchione, K. E., Fletcher, J. M., Lyon, G. R., & Gore, J. C. (2002). Disruption of posterior brain systems for reading in children with developmental dyslexia. *Biol Psychiatry, 52*(2), 101-110.

Shaywitz, S. E. (2003). *Overcoming dyslexia: A new and complete science based program for reading problems at any level*. New York: Alfred A. Knopf.

Shaywitz, B. A., Lyon, G. R., & Shaywitz, S. E. (2006). The role of functional magnetic resonance imaging in understanding reading and dyslexia. *Dev Neuropsychol, 30*(1), 613-632.

Shaywitz, S. E., & Shaywitz, B. A. (2008). Paying attention to reading: the neurobiology of reading and dyslexia. *Dev Psychopathol, 20*(4), 1329-1349.

Siok , W. T., & Flechter, P. (2001). The role of phonological awareness and visual–orthographic skills in Chinese reading acquisition. *Developmental Psychology, 37*, 886–899.

Skottun, B. C. (2000). The magnocellular deficit theory of dyslexia: the evidence from contrast sensitivity. *Vision Res, 40*(1), 111-127.

Snow, C. E., Burns, M. S., & Griffin, P. (1998). *Preventing Reading Difficulites in Children*. Sahington: National Academy Press.

Snowling, M. J. (1987). *Dyslexia: A Cognitive Developmental Perspective*. Oxford: Blackwell.

Snowling, M., Chiat, S., & Hulme, C. (1991). Words, nonwords, and phonological processes: Some comments on Gathercole, Willis, Emslie and Baddeley. *Applied Psycholinguistics, 12*(369-373).

Snowling, M., Bishop, D. V., & Stothard, S. E. (2000a). Is preschool language impairment a risk factor for dyslexia in adolescence? *J Child Psychol Psychiatry, 41*(5), 587-600.

Snowling, M. J., Bishop, D. V., & Stothard, S. E. (2000b). Is preschool language impairment a risk factor for dyslexia in adolescence? *Journal of Child Psychology and Psychiatry, 41*(5), 587-600.

Specht, K., Osnes, B., & Hugdahl, K. (2009). Detection of differential speech-specific processes in the temporal lobe using fMRI and a dynamic "sound morphing" technique. *Hum Brain Mapp, 30*(10), 3436-3444.

Spironelli, C., & Angrilli, A. (2009). Developmental aspects of automatic word processing: language lateralization of early ERP components in children, young adults and middle-aged subjects. *Biol Psychol, 80*(1), 35-45.

Sprenger-Charolles, L., Siegel, L. S., Bechennec, D., & Serniclaes, W. (2003). Development of phonological and orthographic processing in reading aloud, in silent reading, and in spelling: a four-year longitudinal study. *J Exp Child Psychol, 84*(3), 194-217.

Stainthorp, R., & Hughes, D. (1998). Phonological sensitivity and reading: evidence from precocious readers. *Journal of Research in Reading, 21*(1), 53-68.

Stanford, T. R., & Stein, B. E. (2007). Superadditivity in multisensory integration: putting the computation in context. *Neuroreport, 18*(8), 787-792.

Stein, J., & Walsh, V. (1997). To see but not to read; the magnocellular theory of dyslexia. *Trends Neurosci, 20*(4), 147-152.

Stein, J. (2001). The magnocellular theory of developmental dyslexia. *Dyslexia, 7*(1), 12-36.

Steinbrink, C., Vogt, K., Kastrup, A., Muller, H. P., Juengling, F. D., Kassubek, J., & Riecker, A. (2008). The contribution of white and gray matter differences to developmental dyslexia: insights from DTI and VBM at 3.0 T. *Neuropsychologia, 46*(13), 3170-3178.

Steinbrink, C., Ackermann, H., Lachmann, T., & Riecker, A. (2009). Contribution of the anterior insula to temporal auditory processing deficits in developmental dyslexia. *Hum Brain Mapp, 30*(8), 2401-2411.

Steingruber, H. J. (1971). *Hand-Dominanz-Test (HDT)*. Göttingen, Toronto, Zürich: Verlag für Psychologie Dr. C. J. Hogrefe.

Stevenson, J., Graham, P., Fredman, G., & McLoughlin, V. (1987). A twin study of genetic influences on reading and spelling ability and disability. *J Child Psychol Psychiatry, 28*(2), 229-247.

Stoodley, C. J., Talcott, J. B., Carter, E. L., Witton, C., & Stein, J. F. (2000). Selective deficits of vibrotactile sensitivity in dyslexic readers. *Neurosci Lett, 295*(1-2), 13-16.

Strik, W. K., Fallgatter, A. J., Brandeis, D., & Pascual-Marqui, R. D. (1998). Three-dimensional tomography of event-related potentials during response inhibition: evidence for phasic frontal lobe activation. *Electroencephalogr Clin Neurophysiol, 108*(4), 406-413.

Svensson, I., & Jacobson, C. (2006). How persistent are phonological difficulties? A longitudinal study of reading retareded children. *Dyslexia, 12*, 2-3.

Tabuchi, M., Fujii, T., Suzuki, K., Endou, K., & Yamadori, A. (2000). [Effect of number of syllables in word repetition]. *No To Shinkei, 52*(1), 29-35.

Talairach, J., & Tournoux, P. (1988). *Co-Planer Stereotaxic Atlas of the Human Brain*. Stuttgart: Georg Thieme Verlag.

Tallal, P. (1980). Auditory temporal perception, phonics, and reading disabilities in children. *Brain Lang, 9*(2), 182-198.

Tallal, P. (2004). Improving language and literacy is a matter of time. *5*(9), 721-728.

Tallal, P., & Gaab, N. (2006). Dynamic auditory processing, musical experience and language development. *Trends Neurosci, 29*(7), 382-390.

Tanaka, J. W., & Curran, T. (2001). A neural basis for expert object recognition. *Psychol Sci, 12*(1), 43-47.

Tarkiainen, A., Helenius, P., Hansen, P. C., Cornelissen, P. L., & Salmelin, R. (1999). Dynamics of letter string perception in the human occipitotemporal cortex. *Brain, 122 (Pt 11)*, 2119-2132.

Temple, E. (2002). Brain mechanisms in normal and dyslexic readers. *Curr Opin Neurobiol, 12*(2), 178-183.

Temple, E., Deutsch, G. K., Poldrack, R. A., Miller, S. L., Tallal, P., Merzenich, M. M., & Gabrieli, J. D. (2003). Neural deficits in children with dyslexia ameliorated by behavioral remediation: evidence from functional MRI. *Proc Natl Acad Sci U S A, 100*(5), 2860-2865.

Tewes, U., & Rossmann, P. U. S. (1999). *Hamburg-Wechsler-Intelligenztest für Kinder*. Bern: Verlag Hans-Huber.

Tewes, U. (2001). *HAWIE-R Hamburger-Wechsler Intelligenztest für Erwachsene Revision 1991*. Bern: Hans Huber Verlag.

Thompson, R. F., Johnson, R. H., & Hoopes, J. J. (1963). Organization of auditory, somatic sensory, and visual projection to association fields of cerebral cortex in the cat. *J Neurophysiol, 26*, 343-364.

Torgesen, J. K., Wagner, R. K., Rashotte, C. A., Burgess, S., & Hecht, S. (1997). Contributions of Phonological Awareness and Rapid Automatic Naming Ability to the Growth of Word-Reading Skills in Second-to Fifth-Grade Children. *Scientific Studies of Reading, 1*(2), 161-185.

Treiman, R. (1985). Phonemic analysis, spelling, and reading. *New Directions for Child and Adolescent Development*(27), 5-18.

Tsapkini, K., & Rapp, B. The orthography-specific functions of the left fusiform gyrus: evidence of modality and category specificity. *Cortex, 46*(2), 185-205.

Turkeltaub, P. E., Eden, G. F., Jones, K. M., & Zeffiro, T. A. (2002). Meta-analysis of the functional neuroanatomy of single-word reading: method and validation. *Neuroimage, 16*(3 Pt 1), 765-780.

Turkeltaub, P. E., Gareau, L., Flowers, D. L., Zeffiro, T. A., & Eden, G. F. (2003). Development of neural mechanisms for reading. *Nat Neurosci, 6*(7), 767-773.

Turkeltaub, P. E., & Coslett, B. H. (2010). Localization of sublexical speech perception components. *Brain and Language, 114*(1), 1-15.

van Atteveldt, N., Formisano, E., Goebel, R., & Blomert, L. (2004). Integration of letters and speech sounds in the human brain. *Neuron, 43*(2), 271-282.

van Atteveldt, N., Formisano, E., Blomert, L., & Goebel, R. (2007a). The effect of temporal asynchrony on the multisensory integration of letters and speech sounds. *Cereb Cortex, 17*(4), 962-974.

van Atteveldt, N. M., Formisano, E., Goebel, R., & Blomert, L. (2007b). Top-down task effects overrule automatic multisensory responses to letter-sound pairs in auditory association cortex. *Neuroimage, 36*(4), 1345-1360.

van der Mark, S., Bucher, K., Maurer, U., Schulz, E., Brem, S., Buckelmüller, J., Kronbichler, M., Loenneker, T., Klaver, P., Martin, E., & Brandeis, D. (2009). Children with dyslexia lack multiple specializations along the visual word-form (VWF) system. *Neuroimage, 47*(4), 1940-1949.

Van Ingelghem, M., van Wieringen, A., Wouters, J., Vandenbussche, E., Onghena, P., & Ghesquiere, P. (2001). Psychophysical evidence for a general temporal processing deficit in children with dyslexia. *Neuroreport, 12*(16), 3603-3607.

Vellutino, F. R., Steger, J. A., Harding, C. J., & Phillips, F. (1975). Verbal vs non-verbal paired-associates learning in poor and normal readers. *Neuropsychologia, 13*(1), 75-82.

Vellutino, F. R., Fletcher, J. M., Snowling, M. J., & Scanlon, D. M. (2004). Specific reading disability (dyslexia): what have we learned in the past four decades? *J Child Psychol Psychiatry, 45*(1), 2-40.

Victor, J. D., Conte, M. M., Burton, L., & Nass, R. D. (1993). Visual evoked potentials in dyslexics and normals: failure to find a difference in transient or steady-state responses. *Vis Neurosci, 10*(5), 939-946.

Vidyasagar, T. R. (1999). A neuronal model of attentional spotlight: parietal guiding the temporal. *Brain Res Brain Res Rev, 30*(1), 66-76.

Vidyasagar, T. R., & Pammer, K. (2010). Dyslexia: a deficit in visuo-spatial attention, not in phonological processing. *Trends Cogn Sci, 14*(2), 57-63.

Vigneau, M., Beaucousin, V., Herve, P. Y., Jobard, G., Petit, L., Crivello, F., Mellet, E., Zago, L., Mazoyer, B., & Tzourio-Mazoyer, N. (2011). What is right-hemisphere contribution to phonological, lexico-semantic, and sentence processing? Insights from a meta-analysis. *Neuroimage 54(1),*577-93.

Weintraub, S., & Mesulam, M. M. (1983). Developmental learning disabilities of the right hemisphere. Emotional, interpersonal, and cognitive components. *Arch Neurol, 40*(8), 463-468.

Wheeler, M. E., Petersen, S. E., & Buckner, R. L. (2000). Memory's echo: vivid remembering reactivates sensory-specific cortex. *Proc Natl Acad Sci U S A, 97*(20), 11125-11129.

Wimmer, H., Hutzler, F., & Wiener, C. (2002). Children with dyslexia and right parietal lobe dysfunction: event-related potentials in response to words and pseudowords. *Neuroscience Letters, 331*(3), 211-213.

Witton, C., Talcott, J. B., Hansen, P. C., Richardson, A. J., Griffiths, T. D., Rees, A., Stein, J. F., & Green, G. G. (1998). Sensitivity to dynamic auditory and visual stimuli predicts nonword reading ability in both dyslexic and normal readers. *Curr Biol, 8*(14), 791-797.

Witton, C., Stein, J. F., Stoodley, C. J., Rosner, B. S., & Talcott, J. B. (2002). Separate influences of acoustic AM and FM sensitivity on the phonological decoding skills of impaired and normal readers. *J Cogn Neurosci, 14*(6), 866-874.

Wolf, M. (1986). Rapid alternating stimulus naming in the developmental dyslexias. *Brain Lang, 27*(2), 360-379.

Wolff, P. H., Michel, G. F., & Ovrut, M. (1990). Rate variables and automatized naming in developmental dyslexia. *Brain Lang, 39*(4), 556-575.

World Health Organization. (1993). *ICD-10. The international classification of diseases*. Geneva: World Health Organization.

World Health Organization. (2009). *ICD-10. The international classification of diseases* (Vol. 10). Bern, Göttingen, Toronto, Seatle.

Wydell, T. N., Vuorinen, T., Helenius, P., & Salmelin, R. (2003). Neural Correlates of Letter-String Length and Lexicality during Reading in a Regular Orthography. *Journal of Cognitive Neuroscience, 15*(7), 1052-1062.

Zaehle, T., Geiser, E., Alter, K., Jancke, L., & Meyer, M. (2008). Segmental processing in the human auditory dorsal stream. *Brain Res, 1220*, 179-190.

Zaehle, T., Jancke, L., Herrmann, C., & Meyer, M. (2009). Pre-attentive Spectro-temporal Feature Processing in the Human Auditory System, *Brain Topography* (22, 97-108): Springer New York.

Zatorre, R. J., & Belin, P. (2001). Spectral and temporal processing in human auditory cortex. *Cereb Cortex, 11*(10), 946-953.

Zatorre, R. J., & Gandour, J. T. (2008). Neural specializations for speech and pitch: moving beyond the dichotomies. *Philos Trans R Soc Lond B Biol Sci, 363*(1493), 1087-1104.

Zeffiro, T., & Eden, G. (2001). The cerebellum and dyslexia: perpetrator or innocent bystander? *Trends Neurosci, 24*(9), 512-513.

Ziegler, J. C., & Goswami, U. (2005). Reading acquisition, developmental dyslexia, and skilled reading across languages: a psycholinguistic grain size theory. *Psychol Bull, 131*(1), 3-29.

Zimmermann, P., Gondan, M., & Fimm, B. (2002). KITAP Testbatterie zur Aufmerksamkeitsprüfung für Kinder. Herzogenrath: Psytest, Vera Fimm, Psychologisches Testsysteme.

11 Appendix

Table 14: Words and Pseudowords Used for Experiment I

Abzug	Gubaz	Labor	Barlo
Adler	Ralde	Läden	Dänle
Allee	Leela	Leben	Neleb
Alter	Relta	Lehre	Herle
Anbau	Aubna	Leute	Teule
Äpfel	Pfelä	Linie	Nilie
Armut	Turma	Löhne	Nöhle
Ärzte	Tärze	Lücke	Celük
Bälle	Lälbe	Magen	Gamen
Beine	Neibe	Marke	Karme
Bogen	Negbo	Masse	Semsa
Bügel	Gülbe	Möbel	Bömel
Bühne	Nühbe	Motor	Romto
Busse	Subse	Motto	Tomto
Eisen	Siene	Mühle	Hülme
Fähre	Herfä	Natur	Ranut
Falle	Lafel	Opfer	Foper
Farbe	Barfe	Osten	Tonse
Figur	Gifur	Paare	Repaa
Flüge	Gülfe	Paket	Takep
Frage	Garef	Pause	Aupes
Gasse	Sagse	Pokal	Kalop
Gäste	Tegäs	Probe	Borpe
Gehör	Regöh	Räder	Därre
Güter	Rütge	Rasen	Nasre
Halle	Lehla	Reihe	Hiere
Hände	Dehnä	Rolle	Loler
Härte	Tehrä	Säcke	Kesäc
Haupt	Tauph	Seite	Tiese
Hitze	Zhite	Söhne	Hönse
Hörer	Reröh	Sonne	Nonse
Hürde	Dürhe	Tänze	Zentä
Jäger	Gäjer	Täter	Rätet
Jubel	Bulje	Thema	Tahme
Kamin	Manki	Tiefe	Feite
Kasse	Saske	Tonne	Nonte
Kette	Tekte	Vater	Taver
Klima	Mikla	Vogel	Gelov
Kohle	Holke	Vögel	Gölve
Köpfe	Peköf	Wärme	Merwä
Krone	Ronke	Welle	Lelew
Kugel	Gelku	Wiese	Siewe
Kunde	Nekdu	Witwe	Tiwew
Kurve	Rukev	Wolke	Kolwe
Küste	Stekü	Wüste	Stüwe

Table 15: Stimuli Used for Experiment II

Abscheu	Feier	Konsum	Reise
Absicht	Fenster	Kopie	Rennen
Abstand	Fülle	Krankheit	Respekt
Ampel	Gage	Lehrer	Satan
Anstieg	Gebiet	Lüge	Säugling
Antrieb	Gegend	Mädchen	Sender
Antwort	Geschenk	Mangel	Sitte
Ärger	Gestalt	Miene	Speise
Aufbau	Gewehr	Mode	Sportler
Aussicht	Gewicht	Modell	Sprecher
Beleg	Grippe	Mütze	Strasse
Betrag	Gruppe	Nachricht	Streit
Betrug	Gürtel	Nummer	Treppe
Bombe	Heirat	Nutzen	Übung
Brille	Hitze	Objekt	Umbruch
Dessert	Hotel	Ordner	Unglück
Dichter	Idee	Pause	Vorteil
Eile	Klausur	Pfeiler	Wiese
Elend	Kleidung	Pflanze	Zeugnis
Fahne	Kneipe	Pflege	Zweifel

Table 16: Words and Pseudowords Used for Experiment III

Allee	Leela	Marke	Karme
Anbau	Aubna	Motor	Romto
Beine	Neibe	Motto	Tomto
Bühne	Nühbe	Osten	Tonse
Farbe	Barfe	Paket	Takep
Frage	Garef	Pokal	Kalop
Hitze	Zhite	Probe	Borpe
Kamin	Manki	Sonne	Nonse
Kette	Tekte	Tänze	Zentä
Kohle	Holke	Thema	Thame
Krone	Ronke	Tiefe	Feite
Leben	Neleb	Tonne	Nonte
Lehre	Herle	Vater	Taver
Lücke	Celük	Vogel	Gelov
Magen	Gamen	Wüste	Stüwe

Professional, Research and Clinical Experience

08.2010 – Present	Assistance in school psychological service (50%), Zurich, Switzerland
08.1998 – Present	Guest Teacher: Typical and Special Needs Classrooms, Switzerland, Cantons of St. Gallen, Thurgau and Zurich, Switzerland
01.2007 – 06.2007	Research Associate (100%) in the field of developmental dyslexia, interdisciplinary project at the ETH Computer Science, Zurich, Switzerland Supervisor: Prof. Dr. Markus Gross
01.2006 – 12.2006	Research Associate (20%) in the field of developmental dyslexia, interdisciplinary project at the ETH Computer Science, Zurich, Switzerland Supervisor: Prof. Dr. M. Gross
12.2005 – 12.2006	ESPAS Group Leader; Foundation for Social and Economic Reintegration of the Impaired, Zurich, Switzerland
07.2004 – 12.2004	Paid Intern: INDB - Institute for Neuropsychological Diagnostics and Imaging, Swiss Epilepsy Center, Zurich, Switzerland Supervisor: Dr. rer. nat. H. Jokeit
08.2002 – 07.2004	Primary School Teacher (Part Time) Zurich, Switzerland

Teaching Experience

06.2010	Supervision oft he module „Neurobiologische Grundlagen der Dyslexie und Auswirkungen auf der kognitiven Ebene“ at the Hochschule für Heilpädagogik (HfH) Zurich, Switzerland
04.2009	Supervision oft he module „Dybuster: Einblick in ein multimediales Rechtschreib-Lernsystem“ at the Pädagogische Hochschule Kreuzlingen, Switzerland
03.2009	Supervision oft he module „Neurobiologische Grundlagen der Dyslexie und Auswirkungen auf der kognitiven Ebene“ at the Hochschule für Heilpädagogik (HfH) Zurich, Switzerland
04.2008	Supervision oft he module „Dybuster: Einblick in ein multimediales Rechtschreib-Lernsystem“ at the Pädagogische Hochschule Kreuzlingen, Switzerland

Member of Scientific Associations

ZNZ Neuroscience Center Zurich

Peer – reviewed Publications

Kast, M., Meyer, M., Vogeli, C., Gross, M., Jancke, L. (2007). Computer-based multisensory learning in children with developmental dyslexia. Restorative Neurology and Neuroscience 25 (2-3), 355-369

Kast, M., Elmer, S., Jancke, L., Meyer, M. (2010). ERP differences of pre-lexical processing between dyslexic and non-dyslexic children. International Journal of Psychophysiology, 77, 59-69.

Kast, M., Baschera, G. M., Gross, M., Jäncke, L. & Meyer, M. Computer based learning of spelling skills in children with and without dyslexia (submitted to Annals of Dyslexia)

Kast, M., Elmer, S., Blättler, F., Jancke, L., Meyer, M. Impaired Audiovisual Integration of Linguistic Contents in Dyslexic Adults.

Kast, M., Bezzola, L, Jäncke, L. & Meyer, M. Multi- and unisensory decoding of words and nonwords result in differential brain responses in dyslexic and non-dyslexic adults (submitted to Brain and Language)

Congress Posters / Abstracts

Conference of Human Brain Mapping, Barcelona, 2010: "Impaired Integration of Linguistic Contents in Dyslexic Adults", Kast, M., Elmer, S., Blättler, F., Jäncke, L. & Meyer, M

Zentrum für Neurowissenschaften Zürich, 2009: "ERP Differences of Prelexical Processing between Dyslexic and Non-dyslexic Children", Kast, M., Elmer, S., Jäncke, L. & Meyer, M

Conference of Human Brain Mapping, San Franciso, 2010: "ERP Differences of Prelexical Processing between Dyslexic and Non-dyslexic Children", Kast, M., Elmer, S., Jäncke, L. & Meyer, M

Congress Talk / Abstract

Kongress des Bundesverbandes Legasthenie & Dyskalkulie, Berlin, 2008, „Verbesserte Rechtschreibleistung dank multimodaler Lernsoftware – Eine Benutzerstudie"

Fundings

11.2007 - 10.2010	Research Funding of the University of Zurich (56234102): PhD position at Prof. Lutz Jäncke's lab, Institute of Psyhcology, Division of Neuropsychology, University of Zurich, Switzerland